

# THE *TELESPOT* PROJECT

IMPLEMENTATION OF A TELEDERMOSCOPY SYSTEM  
IN PRIMARY HEALTHCARE CENTERS  
FOR EARLY SKIN CANCER DETECTION



This thesis is presented in partial fulfilment of the requirements for the title of  
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## Disclaimer

A written consent was obtained for all the clinical pictures presented in this manuscript.

## Abbreviations

|        |  |
|--------|--|
| AI     | artificial intelligence                                    |
| AJCC   | American joint committee on cancer                         |
| ALM    | acral lentiginous melanoma                                 |
| AK     | actinic keratosis  |
| BCC    | basal cell carcinoma                                       |
| BRAF   | v-raf murine sarcoma viral oncogene homolog B1             |
| CBCL   | cutaneous B-cell lymphoma                                  |
| CDK4   | cyclin dependent kinase 4                                  |
| CDKN2A | cyclin dependent kinase inhibitor 2A                       |
| CM     | cutaneous melanoma   |
| cSCC   | cutaneous squamous cell carcinoma                          |
| CTCL   | cutaneous T-cell lymphoma                                  |
| DICOM  | digital imaging and communications in medicine             |
| EADO   | European association of dermatology-oncology               |
| EIS    | electrical impedance spectroscopy                          |
| EORTC  | European organization for research and treatment of cancer |
| EPR    | electronic patient record                                  |
| FAMMM  | familial atypical multiple mole-melanoma syndrome          |
| FDA    | food and drug administration                               |
| FHP    | first-line healthcare provider                             |
| FTF    | face-to-face   |
| GDPR   | general data protection regulation                         |
| HHI    | hedgehog inhibitor   |
| HIS    | hospital information system                                |
| HMB-45 | human melanoma black 45                                    |
| HPM    | high-priority management                                   |
| IARC   | international agency for research on cancer                |
| IHC    | immunohistochemistry                                       |
| IaSCC  | locally advanced cutaneous squamous cell carcinoma         |
| LMM    | lentigo maligna melanoma                                   |
| LPM    | low-priority management                                    |
| MART-1 | melanoma antigen recognized by T-cells 1                   |
| MC1R   | melanocortin-1 receptor                                    |
| MCC    | Merkel cell carcinoma                                      |
| mcSCC  | metastatic cutaneous squamous cell carcinoma               |
| MF     | mycosis fungoides  |
| nBCC   | nodular basal cell carcinoma                               |



|         |  |
|---------|--|
| NM      | nodular melanoma                           |
| NMSC    | non-melanoma skin cancer                   |
| NPD     | non-polarized dermoscopy                   |
| OCT     | optical coherence tomography               |
| OTR     | organ transplant recipient                 |
| PACS    | picture archiving and communication system |
| PASI    | psoriasis area and surface index           |
| PCL     | primary cutaneous lymphoma                 |
| pCNKTCL | primary cutaneous NK/T-cell lymphoma       |
| PD      | polarized dermoscopy                       |
| PD-1    | programmed death-1                         |
| PHC     | primary healthcare center                  |
| RCM     | reflectance confocal microscopy            |
| REST    | representational state transfer            |
| RT      | real-time                                  |
| S&F     | store-and-forward                          |
| sBCC    | superficial basal cell carcinoma           |
| SDDI    | sequential digital dermoscopy imaging      |
| SOX-10  | SRY-related HMG-box 10                     |
| SPF     | sun protection factor                      |
| SSE     | skin self-examination                      |
| SSM     | superficial spreading melanoma             |
| TADA    | triage amalgamated dermoscopy algorithm    |
| TBE     | total body examination                     |
| TD      | tele dermatology                           |
| TDS     | teledermoscopy                             |
| TM      | telemedicine                               |
| TNM     | tumor-node-metastasis                      |
| TSCC    | tertiary skin cancer center                |
| UICC    | union for international cancer control     |
| UPF     | UV protection factor                       |
| UV      | ultraviolet                                |
| WHO     | world health organization                  |
| WSI     | whole-slide imaging                        |

## Foreword

The incidence of melanoma and non-melanoma skin cancer (NMSC) is steadily rising over years (Arnold 2022) and leads to an increased workload for first-line healthcare providers (FHP) and dermatologists. Furthermore, the shortage of dermatologists and increased skin cancer awareness of the population lead to increasingly long waiting times, hence hampering rapid diagnosis and management, which potentially worsens prognoses (Coates<sup>1</sup> 2014).

Facing these facts, triage of suspected skin lesions in primary healthcare centers (PHC) could be useful, but FHP often lack faith in their clinical diagnoses (Tensen 2022). Teledermoscopy (TDS), defined as dermoscopic images analyzed at distance using telecommunication technologies, may help to improve the distinction between benign versus malignant skin lesions and consequently speeding up the management of malignant lesions (Coates<sup>2</sup> 2014). Finally, in terms of public health, early diagnosis followed by appropriate management remains the cornerstone of reduced skin cancer morbidity and mortality (Perez 2022).

In 2019, a pilot TDS project named *TELESPOT* (TELEdermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce) was initiated in the French-speaking part of Belgium. Enrolled PHCs acquired dermoscopic images of skin lesions clinically judged as suspicious and sent them remotely to a tertiary skin cancer center (TSCC). After a double reading of both the clinical and dermoscopic images by two dermatologists, the TSCC sent a triage report with as main information the prioritization of lesion management: low-priority management (LPM) versus high-priority management (HPM). For HPM lesions, rapid care in the TSCC was proposed if required by the PHC. The study covered two subsequent periods. The initial period included acquisitions from six PHCs, from September 2019 to August 2020. The extension period included data from the six initial PHCs and from three additional PHCs, from September 2020 to August 2022. In fact, a preliminary evaluation was performed after the initial period. This evaluation focused on the raw screening data and its comparison with previous published studies, as well as the satisfaction scores of both involved parties (FHPs and patients). After having achieved the aims of this pilot phase and after the validation of several studied parameters and encouraging feedback from the initial PHCs, it was decided to extend the duration of the study, the number of cases and the number of PHC. A final evaluation was performed after the extension period. This evaluation focused on the statistical analysis of data and its comparison between different groups according to initial versus additional PHCs and initial period versus extension period.

This thesis is based on three main peer-reviewed publications, three posters presented at international scientific congresses and one oral communication presented at the national Dermatology congress. These publications present the intellectual and technological development of the project, its implementation, and the evaluation of the initial and extension periods.

# Background

## 1. Skin cancers

### 1.1. Definition and epidemiology of skin cancers

#### 1.1.1. *Melanoma*

##### 1.1.1.1. Definition

Melanoma is a proliferation of malignant melanocytes, melanin-producing neural crest-derived cells. Most commonly, the origin is cutaneous, but mucosal or uveal melanomas exist. The minority of cutaneous melanoma (CM) develops on preexisting pigmentary naevi, whereas 70% of CM are considered as *de novo* lesions (Martín-Gorgojo 2018).

##### 1.1.1.2. Epidemiology

Worldwide, about 300.000 cases of melanoma were registered in 2020. The incidence of CM is steadily increasing for decades, especially in European countries (Arnold 2022). This continued rise is partially artificial and explained by better registration strategies and more systematic excision of suspicious lesions (Erdmann 2013). Nonetheless, projections predict that the number of new cases of CM per year will increase by more than 50% from 2020 to 2040 (Arnold 2022).

In Belgium, the number of newly diagnosed melanomas was 3618 cases in 2020. Melanoma is the fifth most frequent cancer. Figure 1 illustrates the incidence of melanoma over time (Belgian Cancer Registry Group 2022). The decrease in 2020 is artificial. Indeed, the COVID-19 pandemic had a serious impact on general and dermatology healthcare in terms of diagnosis, treatment, and follow-up (Gomolin 2020). Nonetheless, a retrospective analysis was performed in our tertiary center evaluating the impact of COVID-19 on new diagnoses of melanoma. In conclusion, a shift in the total of new melanoma cases per month was observed compared to previous years but no statistically difference in global number of melanoma or stratification was highlighted, possibly explained by the early publication of dermatology care recommendations as well as the rapid onset of teledermatology consultations and surgery services for cases with a high priority management (Gedeah 2021).

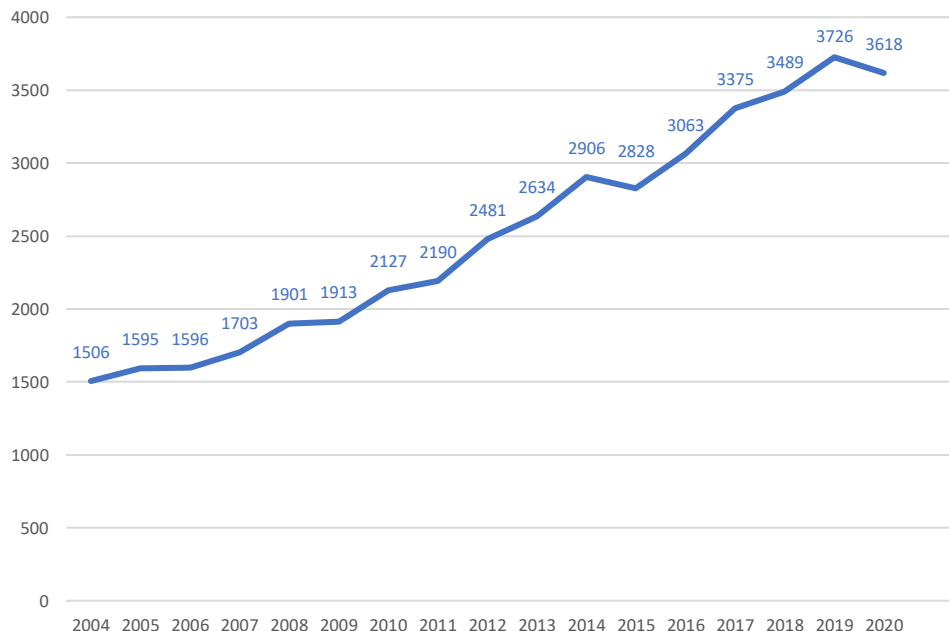


Figure 1 – Incidence of melanoma in Belgium from 2004 to 2020 (Belgian Cancer Registry Group 2022)

### 1.1.1.3. Risk factors

#### 1.1.1.3.1. Non-modifiable risk factors

##### 1.1.1.3.1.1. *Age and Sex*

Although the incidence of melanoma increases with age, melanoma is one of the cancers that can affect relatively young patients. In Australia, melanoma is the most common cancer among men aged between 15 and 49 years, and among women aged between 15-29 (Australian Institute of Health and Welfare 2016). Figure 2 illustrates the distribution of melanoma according to age in Belgium in 2020 (Belgian Cancer Registry Group 2022).

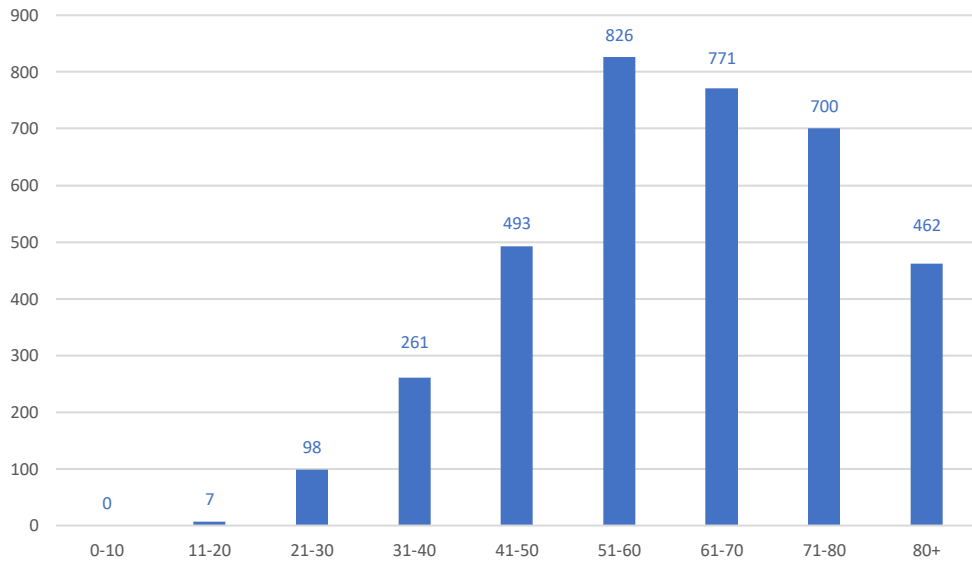


Figure 2 – Distribution of melanoma according to the age group in Belgium in 2020 (Belgian Cancer Registry Group 2022)

Globally, melanoma affects men and women relatively equally, but interesting differences are noticed: men are known to present with less favorable primary tumor features and being a man remains an additional independent predictor of poor outcome (Scoggins 2006). In Belgium, 54.2% of patients with melanoma were women in 2020 (Belgian Cancer Registry Group 2022).

#### 1.1.1.3.1.2. Genetic factors

##### 1.1.1.3.1.2.1. Pigmentation of the skin

The variation in the incidence of melanoma between different ethnic groups is mainly explained by variation in skin and hair color. For similar ultraviolet (UV) exposure, fair skin patients are more likely to develop melanoma (Veirerod 2010). On a molecular scale, variants of melanocortin-1 receptor gene (MC1R) lead to a variable ratio between eumelanin and pheomelanin. The higher the proportion of pheomelanin, the weaker the UV-absorbing properties, which is the stereotypical case of people with red hair (Valverde 1995).

##### 1.1.1.3.1.2.2. Naevi

It is generally accepted that there is a continuous and almost linear increase in risk of melanoma with higher numbers of common melanocytic nevi although studies were performed on patients with variables (regions, skin phototypes, etc.) (Gandini 2005). Thus, the relative risk varies according to regions, from 6.9 in Spain (Rodenas 1997) to 53.9 in Scotland (Swerdlow 1986).

Apart from the total number of naevi, the atypical features of naevi have also been studied as an independent risk factor for melanoma. However, there is no unambiguous definition of atypical naevi. In 1990, the International Agency for Research on Cancer (IARC) proposed a detailed protocol for atypical naevi clinical diagnosis with the following criteria: the presence of a macular component of the lesion in at least one area and the presence of at least three of the following features; not well-defined border, size greater than or equal to 5mm, variegated color, uneven contour, and erythema (Goldstein 2013). These atypical naevi may be sporadic or syndromic, depending on the individual patient. Syndromic cases will be discussed in the “family history of melanoma” section. Sporadic cases are associated with a variable relative risk of melanoma. In contrast to continuous and almost linear increase in risk of melanoma with higher numbers of common melanocytic naevi, a threshold level of five or more atypical naevi was associated with a clearly higher relative risk in several studies (Garbe 1994). The maximum reported relative risk was as high as 32-fold associated with 10 or more atypical naevi (Goldstein 2013).

#### 1.1.1.3.1.2.3. Familial history of melanoma

About 7-15% of melanoma cases are occurring within a familial context. This observation does not necessarily mean that a single genetic mutation is found for each familial history. However, almost half of these familial cases are associated with germline mutations in cyclin dependent kinase inhibitor 2A (CDKN2A) or cyclin dependent kinase 4 (CDK4) (Soura 2016). In addition, certain syndromes have been identified. The best-known is the familial atypical multiple mole-melanoma syndrome (FAMMM syndrome) characterized by the presence of multiple melanocytic naevi and a family history of melanoma as well as, in a subset of patients, an increased risk of developing other malignancies such as pancreatic cancer (Lynch 1968). Overall, a history of melanoma in a first-degree relative approximatively doubles a patient’s lifetime risk (Gandini 2005).

#### 1.1.1.3.1.2.4. Personal history of melanoma

Patients with a personal history of melanoma are at risk of developing subsequent melanomas. This risk is higher in comparison with the risk of developing a first CM in the general population. Among patients with a personal history of melanoma, the frequency of multiple primary melanoma ranges from 0.2% to 12.7% (Veronesi 1976). In a Belgian single center cohort, the incidence of multiple primary melanomas was 2.5%. A younger age at first diagnosis was identified as a risk factor for developing subsequent melanomas. Furthermore, patients with multiple primary melanomas had a worse overall survival compared to patients with single primary melanoma (Absil 2023).

### 1.1.1.3.2. Modifiable risk factors

#### 1.1.1.3.2.1. *UV exposure*

Solar or artificial sources of UV radiation are known to be carcinogenic for humans (El Ghissassi 2009). According to the pattern of UV exposure, the association with melanoma may be stronger or weaker. Intermittent sun exposure, and even more sunburn, is strongly associated with the development of melanoma, particularly during infancy. It appears a linear dose-response association between the number of sunburns and risk of developing melanoma, independently of the age at which the sunburn occurred (Dennis 2008). Chronic and occupational sun exposures are weakly associated with melanoma although this pattern is taken into account in the total exposure modifying the overall risk ((Veirerod 2010).

Geography is a factor affecting exposure of sun radiation. Australia is a particularly interesting case. Indeed, melanoma rates increase with decreasing latitude in the same country (Buettner 2008).

Artificial sources of UV radiations for tanning (sunbeds) are significantly associated with a risk of melanoma. This risk increases with the number of sunbed sessions and the early age of artificial tanning. For patients under 35 years old using sunbeds, the relative risk is increased by a 1.6-fold (Boniol 2012). The same has been demonstrated for patients having been exposed to high-dose and long-term UV therapy for recalcitrant and recurrent psoriasis (Thatiparthi 2022).

#### 1.1.1.3.2.2. *Immunosuppression*

Any situation of immunodepression is associated with an increased cancer risk. In the case of melanoma, the most studied situation is the risk in organ transplant recipients (OTR), with an estimated relative increased risk of 2 to 4 (Vajdic 2009).

### 1.1.2. *Non-melanoma skin cancers*

Non-melanoma skin cancer comprises the different types of basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC). These entities are also currently termed as keratinocyte cancers (Badiu 2023).

#### 1.1.2.1. Basal cell carcinoma

BCC is the most common malignant tumor in fair skin patients and represents about 90% of the NMSC (Cameron<sup>1</sup> 2019, Cameron<sup>2</sup> 2019, Seidl 2021). The incidence of BCC rises with age and is increasing each decade (Wu 2013). In 2018, about 30.000 BCCs were registered in Belgium (Belgian Cancer Registry Group 2022). The life-time risk of BCC in fair skin patients is about 30%. UV exposure is the predominant

modifiable risk factor, but others have been described: ionizing radiation, chemical exposures, and immunosuppression. In fact, the total incidence of BCC increases around 6 times in immunocompromised patients (Wu 2013).

BCC arises from an abnormal and uncontrolled growth of basal keratinocytes in the epidermis (Cameron<sup>2</sup> 2019).

#### 1.1.2.2. Cutaneous squamous cell carcinoma

cSCC is the second most frequent NMSC, after BCC. The incidence of cSCC rises with age and is also increasing with each decade (Que 2018, Stratigos 2015, Stratigos 2020). In 2018, about 8000 cSCCs were registered in Belgium (Belgian Cancer Registry Group 2022). UV exposure is the predominant modifiable risk factor, but others have been described: ionizing radiation, chemical exposures especially arsenic, human papillomavirus infection, and immunosuppression. In fact, the total incidence of cSCC increases between 100 and 250 times in immunocompromised patients (Amaral 2019).

cSCC derives from the spindle cell layer of the epidermis. Actinic keratosis (AK) is the precursor lesion of cSCC. Field cancerization represents the concept that multiple heterogenous genetic mutations may arise in an area exposed to chronic carcinogenic factors. Field cancerization is defined as the anatomical area including or adjacent to AKs with visibly photodamaged skin (pigmentary changes, atrophy and/or telangiectasia) with a significant risk of developing cSCC (Huang 2019).

#### 1.1.2.3. Other skin cancers

This heterogenous group represents less than 1% of skin cancers (Belgian Cancer Registry Group 2022).

##### 1.1.2.3.1. Merkel cell carcinoma

Merkel cell carcinoma (MCC) is a proliferation of malignant anaplastic cells sharing anatomopathological features with cells derived from neuroectoderm, including cutaneous Merkel cells (Coggshall 2018). Global incidence of MCC is estimated at 0.1 to 1.6 cases per 100.000 people per year. Known risk factors include UV exposure, aging, and immunosuppression (Walsh 2021). MCC display nonspecific clinical characteristics and aggressive behavior (Hernandez 2022). Human Polyomavirus infection plays an important role in the carcinogenic process of MCC.

##### 1.1.2.3.2. Primary cutaneous lymphomas

Primary cutaneous lymphomas (PCL) are defined as proliferations of malignant lymphocytes confined to the skin at the initial presentation. It is the third type of lymphoma after hematological and digestive lymphomas. It represents 3.9%



of all non-Hodgkin's lymphomas (Jawed 2014). The European Organization for Research and Treatment of Cancer (EORTC) classification of PCLs is based on clinical, histopathological and immunohistochemical criteria. Two main groups are defined: cutaneous T-cell lymphomas (CTCL) or primary cutaneous NK/T-cell lymphomas (pCNKTCL) representing 75% of PCLs and cutaneous B-cell lymphomas (CBCL) representing 25% of PCLs. Among CTCLs, mycosis fungoides (MF) is the most prevalent (75% of CTCLs and 50% of PCLs).

### 1.1.2.3.3. Others

For information purposes, other rare skin cancers exist, which can develop from any skin structure (adnexal malignant neoplasms, malignant vascular neoplasms, etc.).

## 1.2. Diagnosis of skin cancers

### 1.2.1. Clinical diagnosis

#### 1.2.1.1. Melanoma

Historically, four major clinicopathological subtypes of invasive melanoma have been described (Garbe 2022). Although this classification is not included in the 8<sup>th</sup> edition of the American Joint Committee on Cancer (AJCC) staging system for melanoma, it remains of interest in the clinical diagnosis of melanoma.

#### 1.2.1.1.1. Superficial spreading melanoma

Superficial spreading melanoma (SSM) is the most common clinical subtype, characterized by an initial horizontal growth phase followed by an invasive vertical one (Garbe 2022). Thus, SSM is the clinical prototype used to develop the ABCDE rule, illustrated in figure 3. Sensitivity and specificity of ABCDE rule were estimated at 73.1% and 77.8%, respectively. However, the performance of this algorithm falls significantly in the case of other clinical presentations of melanoma (Benelli 1999).

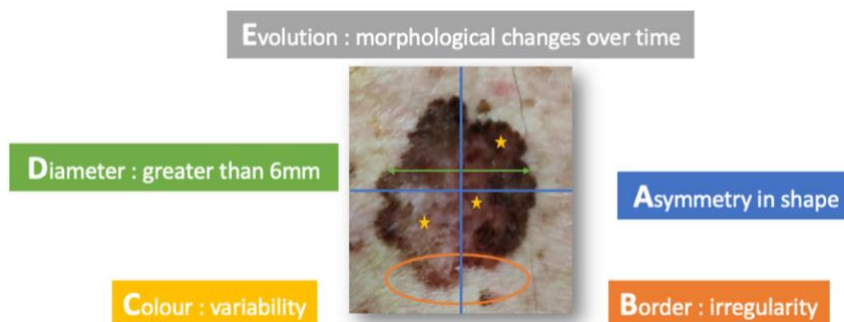


Figure 3 – ABCDE rule for SSM clinical diagnosis

#### 1.2.1.1.2. Nodular melanoma

Nodular melanoma (NM) represents about 15% of melanoma and is poorly detected with ABCDE rule. Indeed, the clinical presentation of NM is usually a dark rapidly growing nodule with more regular borders and homogeneous color in comparison with SSM (figure 4). Moreover, NM is more frequently hypomelanotic, or even amelanotic, making clinical diagnosis even more hazardous (Detrixhe 2018, Dessinioti 2018).



Figure 4 – Nodular melanoma

#### 1.2.1.1.3. Lentigo maligna melanoma

Lentigo maligna melanoma (LMM) is the most common clinical presentation of melanoma on the face and neck (figure 5). This subtype is closely associated with aging population. The ABCDE rule as diagnostic tool is less suitable and hence reliable for LMM diagnosis.



Figure 5 – Lentigo maligna melanoma

#### 1.2.1.1.4. Acral lentiginous melanoma

Acral lentiginous melanoma (ALM) is a rare clinical presentation. It occurs on hairless skin, such as palms, soles, and subungual areas. Clinical features are highly heterogeneous, delaying diagnosis (figure 6). ALM is frequently mistaken for benign dermatosis (warts, nevi, or fungal infections) (Detrixhe 2018, Matas-Nadal 2019).



Figure 6 – Acral lentiginous melanoma

#### 1.2.1.2. Non-melanoma skin cancers

##### 1.2.1.2.1. Basal cell carcinoma

The vast majority of BCCs presents as single lesion, indolent and slowly evolving. This lesion usually appears as a flat, firm, raised, pink or red, translucent area with one or more visible irregular telangiectasia. For more advanced BCCs, these features can also be found: ulcerative area in the center, pigmentation with black-blue areas, oozing or crusted areas. About half of the BCCs are of the nodular subtype (nBCC) (figure 7) whereas 20-30% are superficial (sBCC) (figure 8). Only 5-10% of BCCs are more aggressive subtypes such as sclerodermiform subtype (figure 9) (Cameron<sup>1</sup> 2019, Cameron<sup>2</sup> 2019).



Figure 7 – Nodular basal cell carcinoma



Figure 8 – Superficial basal cell carcinoma



Figure 9 – Sclerodermiform basal cell carcinoma

#### 1.2.1.2.2. Cutaneous squamous cell carcinoma

The vast majority of cSCCs are well differentiated, slowly evolving, hyperkeratotic, isolated lesions, usually developing on areas of field cancerization with multiple AK lesions as illustrated in figure 10 (Que 2018).



Figure 10 – Cutaneous squamous cell carcinoma

### 1.2.2. Dermoscopy

#### 1.2.2.1. Principles of dermoscopy

As described above, “naked eye” examination of the skin lesions is the first essential step in the diagnostic process. However, the high reflective index of the stratum corneum, the most superficial layer of the skin, blocks the visualization of deeper skin structures and is therefore the limiting factor (Braun 2005).

Dermoscopy is a non-invasive imaging technique combining a magnification device and a light source. This enables the visualization of the subsurface morphology of cutaneous lesions, down to the depth of the superficial dermis. Moreover, this reveals colors and structures that are normally not viewable (Menzies<sup>1</sup> 2009). There are two types of dermoscopy: non-polarized (NPD) and polarized (PD), depending on the use of cross-polarized filters. The main difference between NPD and PD is the depth of visualized structures. NPD is best fitted for the examination of structures in the superficial skin layers and PD for the examination of structures in the deeper skin layers (Benvenuto-Andrade 2007). Now, these two types of dermoscopy are combined in a single device which allows toggling from NPD to PD.

### 1.2.2.2. Dermoscopic equipment

As many dermoscopic devices have been developed as there are types of application required.

For daily practice, the handheld dermatoscope is the most used (figure 11). There are also systems that can be adapted to smartphones, tablets, or cameras, enabling images storage (figure 12).

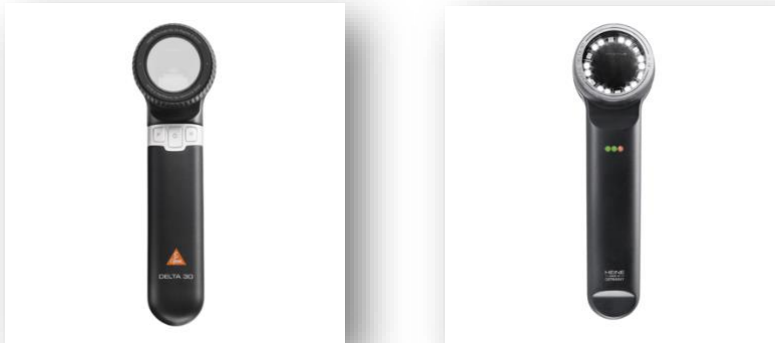


Figure 11 – Handheld dermatoscope (Heine® DELTA 30; Heine Optotechnik, Herrsching, Germany)



Figure 12 – Digital dermatoscope (Heine® iC1; Heine Optotechnik, Herrsching, Germany)

Devices were developed for sequential digital dermoscopy imaging (SDDI) (figure 13). It involves the acquisition and examination of successive dermoscopic images over time. Two settings are performed: short-term digital monitoring (e.g. 3 months interval time) for suspicious lesions and long-term digital monitoring (e.g. 6 to 12 months interval time) (Salerni 2012).



Figure 13 – SDDI system (DermaGraphix®; Canfield Scientific, Parsippany, USA)

Most recently, full body imaging systems have been introduced (figure 14). These systems enable to acquire and organize full body clinical and dermoscopic images. Combined with artificial intelligence (AI), these systems could increase diagnostic performance in the future (Fried 2020).



Figure 14 – Full body imaging system (VECTRA® WB360; Canfield Scientific, Parsippany, USA)

### 1.2.2.3. Application of dermoscopy in oncologic area

#### 1.2.2.3.1. Diagnostic performance

Dermoscopy has demonstrated its added value in terms of diagnostic accuracy of cutaneous tumors. However, its major impact remains to improve the detection of melanoma, compared with “naked eye” examination. One of the latest meta-analyses on the topic showed a relative odds ratio of 15.6 in favor of dermoscopy for primary melanoma diagnosis versus “naked eye” examination. Sensitivity was significantly higher in dermoscopy than in “naked eye” examination, 90% and 71% respectively. Specificity did not appear to be significantly different (Vestergaard 2008). By improving diagnostic accuracy, dermoscopy results in a significant reduction in the ratio of benign to malignant pigmented lesions excised by clinicians. In a prospective clinical study comparing SDDI with “naked eye” examination, the excision rate of benign pigmented lesions was reduced by 63.5% with SDDI (Menzies<sup>2</sup> 2009). Dermoscopy has gradually established itself as a reliable and effective diagnostic tool, requiring dedicated training. Today, it has a grade A recommendation for clinicians who routinely perform skin lesions examination (Garbe 2022), A evidence grade corresponding to consistent evidence from randomized trials, or overwhelming evidence of some other form.

#### 1.2.2.3.2. Diagnostic algorithms

Over time, many dermoscopic algorithms have been developed. Although there are differences in terms of specificity/sensitivity and learning complexity, none of them has been accepted as the gold standard. Clinicians are therefore free to apply the algorithm with which they feel most confident (Carrera 2016).



#### 1.2.2.3.2.1. ABCD rule

The ABCD rule is the first dermoscopic algorithm calculating a probability score that the lesion examined is malignant (Ahnlide 2016). The first three criteria are comparable to the ABCDE rule of “naked eye” examination (asymmetry, border, and color). The last criterium relates to dermoscopic structures and includes: structureless areas, pigment network, branched streaks (atypical network), dots and globules (figure 15).

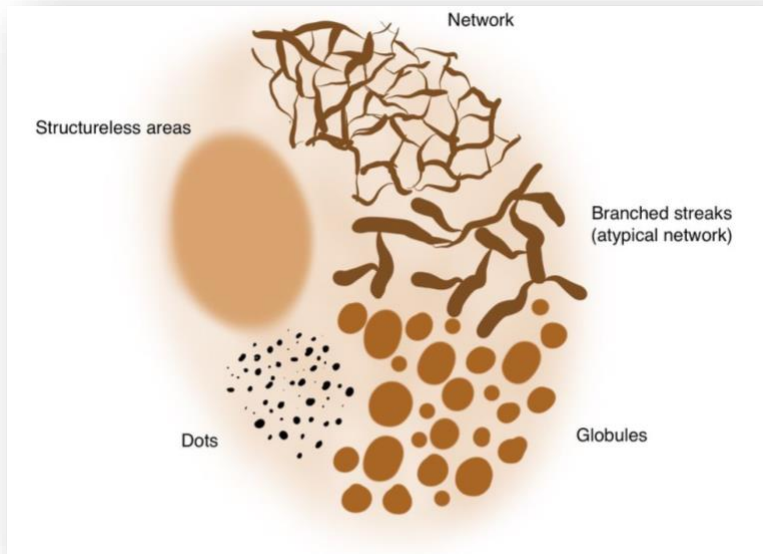


Figure 14 – Dermoscopic structures in dermoscopic ABCD rule  
 (“structureless area schematic” on *dermoscopia.org* website consulted on 18.09.2023)

#### 1.2.2.3.2.2. *Menzies method*

Menzies method is a simplified dermoscopic algorithm based on eleven features scored as present or absent (Menzies 1996). Individual features were selected with low sensitivity for melanoma, defining the two “negative features” (symmetry of pigmentation pattern and single color) and high specificity for melanoma, defining the nine “positive features” (blue-white veil, multiple brown dots, pseudopods, radial streaming, scar-like depigmentation, peripheral black dots/globules, multiple colors, multiple blue-gray dots, and broadened network) (figure 15). According to this algorithm, the diagnosis of melanoma will be made provided there are the two negative criteria and at least one positive criteria.

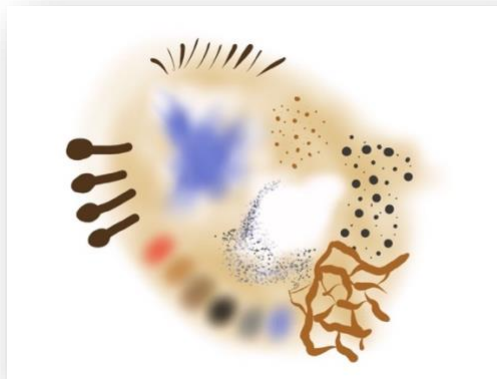


Figure 15 – Positives features in dermoscopic Menzies method  
 (“Menzies method schematics 2” on [dermoscopia.org](http://dermoscopia.org) website consulted on 18.09.2023)

#### 1.2.2.3.2.3. *Seven-point checklist*

The seven-point checklist is one of the most validated dermoscopic algorithms due to its high sensitivity and specificity, also when applied by non-expert clinicians. Seven criteria are separated into major criteria worth 2 points (atypical network, blue-white veil, and atypical vascular pattern) and minor criteria worth 1 point (irregular streaks, irregular dots/globules, irregular blotches, and regression structures). A total score of minimum 3 allows identifying melanoma with a sensitivity of 95% and a specificity of 75% (Argenziano 2011).

#### 1.2.2.3.2.4. *Three-point checklist*

The three-point checklist was initially designed as a screening tool for non-expert clinicians. With its high sensitivity for pigmented cutaneous skin cancer, it enables rapid triage of suspicious pigmented lesions based on three criteria: Asymmetry of pattern and structures, blue-white structures, and atypical network. The threshold is defined by the presence of at least one criterium (Soyer 2004).

1.2.2.3.2.5. *Triage Amalgamated Dermoscopy Algorithm*

The Triage Amalgamated Dermoscopy Algorithm (TADA) is a step-by-step approach with a sensitivity of 94% and a specificity of 72%. It requires basic knowledge on the part of the user in the dermoscopic identification of some lesions (Rogers 2017). The three steps of TADA are illustrated in figure 16.

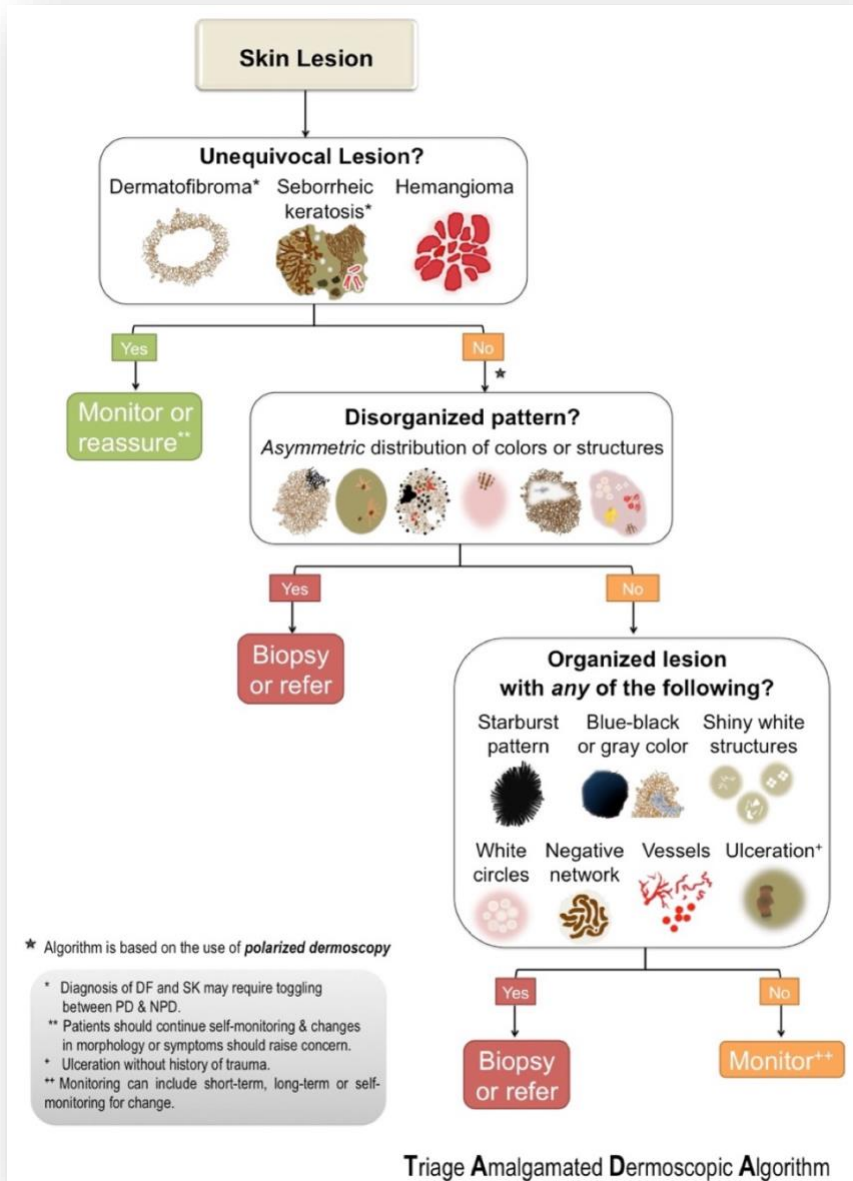


Figure 16 – TADA dermoscopic algorithm  
 ("2017-01 TADA updated" on *dermoscopia.org* website consulted on 18.09.2023)

1.2.2.3.2.6. Revised top-down two-step algorithm

The top-down two-step algorithm is a complete approach to the dermoscopy of most skin tumors (Marghoob 2010). In short, the first step is to establish a specific diagnosis if possible (Figure 17). The second step is to rule out melanoma (Figure 18).

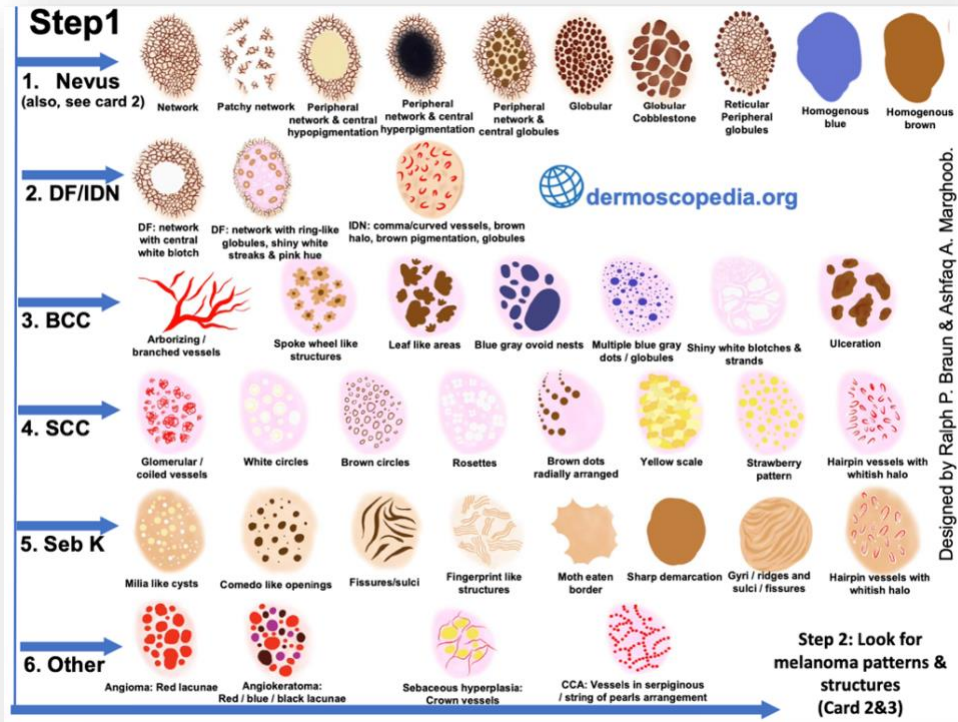
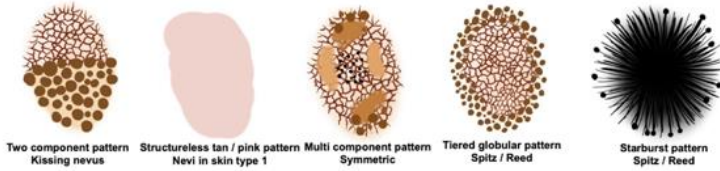


Figure 17 – Step 1 of top-down two-step algorithm: specific diagnosis (“2 step card final” on *dermoscopia.org* website consulted on 18.09.2023)

## Nevus patterns that require context (melanoma should be in the differential)



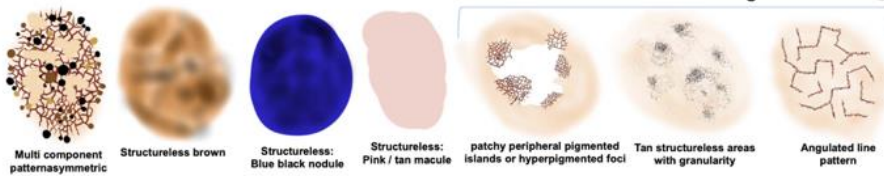
dermoscopia.org

Designed by Ralph P. Braun & Ashfaq A. Marghoob.

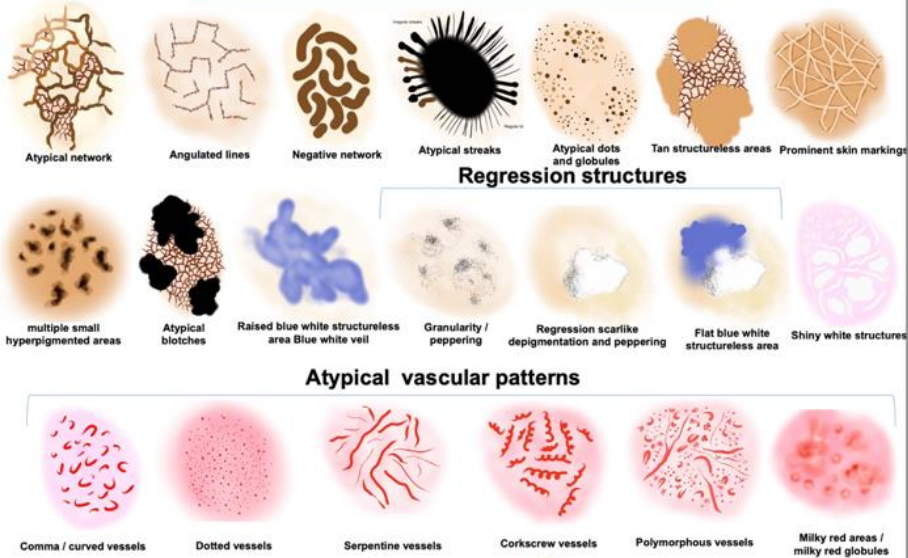
### Melanoma pattern:

1. Do not manifest any of the benign nevus patterns depicted on card 1
2. Usually display a multicomponent disorganized pattern with at least one melanoma specific structure depicted on (Card 3)
3. Can be structureless or featureless or blue-black in color (non-specific or feature-poor)
4. On sun-damaged skin they often appear as large lentiginous lesions with the patterns shown below

#### Melanoma on sun damaged skin



## Melanoma specific structures



Designed by Ralph P. Braun & Ashfaq A. Marghoob

dermoscopia.org



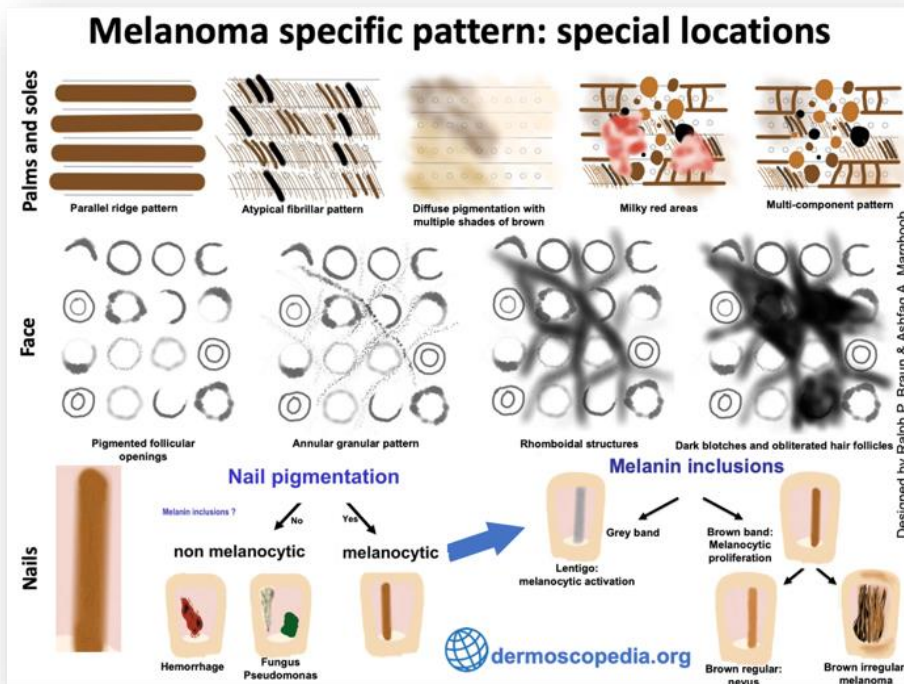


Figure 18 – Step 2 of top-down two-step algorithm: melanoma rule out (“2 step card final” on [dermoscopedia.org](http://dermoscopedia.org) website consulted on 18.09.2023)

#### 1.2.2.4. Application of dermoscopy in non-oncologic area

In addition to its ever-increasing use in dermato-oncology, dermoscopy has also found a place in various other areas of dermatology. By way of example, trichoscopy is defined as the use of dermoscopy in the field of hair disorders, particularly inflammatory conditions. A more common use is the dermoscopic demonstration of scabious burrows in infectious diseases (Sonthalia 2023).

#### 1.2.3. New non-invasive techniques

##### 1.2.3.1. Reflectance confocal microscopy

Reflectance confocal microscopy (RCM) is a non-invasive technology developed in the early 90s for skin imaging. RCM allows to visualize horizontally sectioned images of the skin at a cellular lateral resolution of about 1  $\mu\text{m}$ , to the depth of the upper dermis. The contrast for the monochrome images is obtained by the variation of the optical properties within the skin illuminated by a near-infrared light (830 nm). Melanin offers the greatest contrast, so that RCM is particularly useful for pigmented lesions assessment. Several algorithms have been developed for RCM images interpretation.

In a clinical practice, RCM has value for assessing lesions that are difficult to examine clinically or dermoscopically. In addition, RCM may help to assess amelanotic lesions and tumor surgical limits (Dinnes 2018). The elevated costs of these devices significantly hinder large scale use for skin cancer detection.

#### 1.2.3.2. [Optical coherence tomography](#)

Optical coherence tomography (OCT) is a non-invasive imaging technique originally developed in ophthalmology. Based on the principle of Michelson interferometry, OCT provides two-dimensional images with a resolution of 15  $\mu\text{m}$  and a maximum analysis depth of 1.5 mm (Welzel 2001).

Following numerous studies published since the 90s, OCT has become a reference non-invasive imaging technique in onco-dermatology, particularly for NMSC (Olsen 2018).

#### 1.2.3.3. [Electrical impedance spectroscopy](#)

Electrical impedance spectroscopy (EIS) is a non-invasive imaging technique based on measuring electrical impedance in normal versus abnormal skin. More specifically, these tissues differ in terms of cell size, shape, orientation, compactness, and structure of cell membranes. These differences influence the cellular ability to conduct and store electricity (Braun 2017).

EIS appears to be a complementary tool for difficult-to-assess lesions, especially for clinically suspicious melanocytic lesions (Garbe<sup>2</sup> 2022).

### 1.2.4. [Anatomopathology](#)

If skin cancer is suspected, a relevant histological analysis is required. Understanding the pathology report is essential for appropriate patient management (Thompson 2004).

#### 1.2.4.1. [Melanoma](#)

Accurate diagnosis of a melanocytic lesion requires a comprehensive assessment of the architectural and cellular characteristics. These characteristics are heterogeneous within the same tumor. Histopathological analysis is therefore best performed on the complete tumor sample, also known as an excisional biopsy (McCarthy 2010).

#### 1.2.4.1.1. Concept of radial and vertical growth phase

Radial growth phase is the first stage of development of melanoma. It refers to the intraepidermal proliferation of atypical melanocytes eventually followed by the invasion of papillary dermis. The vertical growth phase is associated with angiogenesis and expression of vascular endothelial growth factor. In some cases, vertical growth phase is not preceded by the radial growth phase, as in NM (Weedon 2010).

This concept is correlated with the binary classification of melanoma: pre-invasive form (also called “melanoma in situ”, including the variant “lentigo melanoma”) and invasive form (Weedon 2010).

#### 1.2.4.1.2. Histopathological categories

Common diagnostic criteria have been established for malignant melanoma (table 1).

| Architectural criteria                   |
|--|
| Asymmetry                                |
| Poor circumscription                     |
| Epidermal nests of melanocytes showing:  |
| Confluence                               |
| Variability in size and shape            |
| Haphazard interval and array             |
| Solitary epidermal melanocytes showing:  |
| Predominance over nests                  |
| Pagetoid spread                          |
| Haphazard arrangement                    |
| Dermal nests showing:                    |
| Variability in size and shape            |
| Confluence                               |
| Lack of maturation in depth              |
| Variability in melanin distribution      |
| Melanocytes within lymphovascular spaces |

| Cytological criteria  |
|-----------------------|
| Nuclear pleomorphism  |
| Nucleolar variability |
| Mitosis:              |
| Even deep             |
| Sometimes atypical    |
| Apoptosis increased   |

Table 1 – Histological criteria for the diagnosis of malignant melanoma according to Ackerman (Ackerman 1994)



Moreover, several histopathological invasive subtypes have been described (Weedon 2010):

- 1) SSM is characterized by a proliferation of atypical melanocytes, singly and in nests, at all levels within the epidermis with pagetoid spread. Superficial adnexal epithelium may also be involved.
- 2) LMM is characterized by an epidermal component of atypical melanocytes, singly and in nests, usually confined to the basal layer and with little pagetoid invasion of the epidermis.
- 3) NM differs by its dominant vertical nodular growth. The dermal component is usually composed of oval to round epithelioid cells.
- 4) ALM has a radial growth phase characterized by a lentiginous pattern of atypical melanocytes, with some nesting.
- 5) Desmoplastic/spindle-cell melanomas are composed of strands of elongated spindle-shaped cells surrounded by mature collagen bundles.

#### 1.2.4.1.3. Immunohistochemistry

In difficult cases of suspected melanoma, special techniques may be useful for increasing diagnostic accuracy. Immunohistochemistry (IHC) is a laboratory technique to identify specific antigens within tissue sections using a dedicated antigen-specific antibody. The various antibodies have a range of sensitivities and specificities and must be interpreted in the context of morphological features (Taylor 2011). Currently, the following antibodies are used for helping to achieve melanoma diagnosis (Weedon 2011):

- 1) S100a protein is not a single protein but a family of over 20 acidic calcium-binding proteins. It remains the most sensitive marker for melanocytic lesions, both benign and malignant.
- 2) SRY-related HMG-box 10 (SOX-10) protein is transcription factor that is also highly sensitive for melanocytic lesions.
- 3) Human melanoma black 45 (HMB-45) protein is a monoclonal antibody reacting against an antigen found in melanocytic tumors. It can be used to distinguish benign nevus and invasive melanoma but is not entirely distinctive. Furthermore, immunostaining is often lost in the deeper aspects of nevus.

- 4) Melanoma antigen recognized by T-cells 1 (MART-1, also abbreviated Melan-A) is a protein antigen demonstrating melanocytic differentiation. A spindle-cell melanocytic lesion that does not express MART-1 is more likely to be a melanoma than a nevus. It is more sensitive than HMB-45 and more specific than stains for S100a protein (Weedon 2010).
- 5) V-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600E antibody has been shown to be highly correlated with the presence of a BRAF V600E mutation within the tumor (Maji 2023). The significance of molecular mutation testing is described in the next section.

#### 1.2.4.1.4. Molecular mutation testing

Current scientific research is particularly interested in characterizing the genetic signature of tumors. These genetic signatures could predict the disease progression or the response to targeted therapies (Maji 2023).

In the case of melanoma, BRAF mutations are the most advanced example. BRAF mutations occur in nearly 50% of all melanomas but more frequently detected in younger patients (Long 2011). Several mutation testing assays exist (Sanger sequencing, allele-specific reverse transcriptase-polymerase chain reaction, pyrosequencing, mass spectroscopy/multiplex assays, ...). Sanger sequencing has traditionally been considered the gold standard (Maji 2023).

#### 1.2.4.1.5. Synoptic reporting

The information in the pathology report is of great importance in guiding clinical management. Communication of this information must therefore be as structured and clear as possible. The synoptic report is a methodical way for complete, easy, and reproducible transmission of the significant features of melanoma. Elements of synoptic reports vary between institutions, but minimum data sets are recommended by consensus guidelines (Scolyer 2013):

- 1) Patient details are mandatory for medico-legal purposes.
- 2) Clinical history includes site of tumor, clinical features of tumor, degree of suspicion of malignancy, history of prior melanoma.
- 3) Macroscopic and microscopic description gives the pathologist the opportunity to express his degree of diagnostic certainty.
- 4) Tumor thickness, commonly termed “Breslow thickness”, is commonly accepted as the most important factor of survival and determines the subsequent work-up and treatment plan. It is defined as the distance from the top of the granular layer of the epidermis to the deepest invasive melanoma

cell. Although still mentioned in histological reports, Clark level has now been superseded by Breslow thickness. Clark level is an expression of the dermal compartment involved by an invasive melanoma. It remains useful when the Breslow thickness cannot be measured (Balch 1978).

- 5) Clinical and histological surgical margins should be measured and reported.
- 6) Ulceration has an adverse prognostic significance, mainly explained by the underestimation of tumor thickness.
- 7) Mitotic rate had an important prognostic significance. However, recent studies have found that the mitotic rate is not an independent prognosticator, and it is significantly associated with tumor thickness and ulceration.
- 8) Satellite deposits, defined as the presence of microscopic satellite deposits separated from the main body of the tumor, have an adverse influence.
- 9) Lymphocytic infiltration is considered as a favorable feature (Weedon 2010).
- 10) Melanoma histopathological subtype is traditionally reported even though it doesn't provide definitive prognostic information. However, there is increasing evidence that these subtypes have different genetic abnormalities with a potential therapeutic impact. For example, LMM has a better prognosis compared to ALM.
- 11) Regression observed clinically as scar-like tissue and histologically as fibrotic areas is considered as good prognostic factor.

#### 1.2.4.2. Non-melanoma skin cancers

##### 1.2.4.2.1. Basal cell carcinoma

Several histopathological subtypes have been defined explained by considerable variability in morphologic features of BCC, but mixed patterns are common (Weedon 2010):

- 1) Nodular (solid) variant is composed of islands of cells with peripheral palisading and a haphazard arrangement of the more central cells.
- 2) Micronodular variant is like solid variant, but nests are much smaller and peripheral palisading is less developed.
- 3) Cystic variant is defined by presence of one or more cystic spaces toward the center of some or all the tumor islands.

- 4) Superficial (multifocal) variant is composed of multiple small islands of basaloid cells attached to the undersurface of the epidermis.
- 5) Pigmented variant is characterized by melanin pigments forms in solid, micronodular, multifocal, superficial, or follicular variants.
- 6) Adenoid variant is defined by thin strands of basaloid cells in a reticulate pattern.
- 7) Infiltrating variant has distinctive histological features such as elongated strands of basaloid cells infiltrating between collagen bundles.
- 8) Sclerosing variant has narrow elongated strands and small islands of tumor cells embedded in a dense fibrous stroma.
- 9) Keratotic variant is like solid variant with squamous differentiation and keratinization in the centers of the islands. These lesions are called basosquamous carcinomas.
- 10) Infundibulocystic variant is characterized by numerous small infundibular cyst-like structures containing keratinous material.
- 11) Metatypical variant is dedicated to rare basal cell carcinoma composed of nests and strands of cells maturing into larger and paler cells.

#### 1.2.4.2.2. Cutaneous squamous cell carcinoma

Commonly, cSCC is histologically defined as nests of squamous epithelial cells which arise from the epidermis and extend variably into the dermis. There is a variable central keratinization and horn pearl formation depending on the tumor differentiation. According to a subjective assessment of differentiation degree, cSCC is classified as well, moderate, or poorly differentiated (Weedon 2010).

### 1.3. Stadification of skin cancers

#### 1.3.1. *Melanoma*

Melanoma is staged according to the Tumor-Node-Metastasis (TNM) classification. Staging helps to estimate the patient's prognosis, choose the most appropriate treatment, standardize information, and makes it easier to compare different groups in terms of survival and support clinical trials (Garbe<sup>2</sup> 2022).

Currently, the AJCC eighth edition of melanoma staging system is the gold standard (table 2).

| T category                       |     | Thickness (mm)             | Ulceration status      |
|----------------------------------|-----|----------------------------|------------------------|
| Tx: cannot be assessed           |     | Not applicable             | Not applicable         |
| T0: no evidence of primary tumor |     | Not applicable             | Not applicable         |
| Tis: melanoma in situ            |     | Not applicable             | Not applicable         |
| T1                               |     | ≤ 1.0                      | Unknown or unspecified |
|                                  | T1a | < 0.8                      | Without ulceration     |
|                                  | T1b | < 0.8                      | With ulceration        |
| 0.8 – 1.0                        |     | With or without ulceration |                        |
| T2                               |     | > 1.0 – 2.0                | Unknown or unspecified |
|                                  | T2a |                            | Without ulceration     |
|                                  | T2b |                            | With ulceration        |
| T3                               |     | > 2.0 – 4.0                | Unknown or unspecified |
|                                  | T3a |                            | Without ulceration     |
|                                  | T3b |                            | With ulceration        |
| T4                               |     | > 4.0                      | Unknown or unspecified |
|                                  | T4a |                            | Without ulceration     |
|                                  | T4b |                            | With ulceration        |

| N category |     | Number of tumor-involved regional lymph nodes   | Presence of in-transit, satellite and/or microsatellite metastases |
|------------|-----|---|--|
| Nx         |     | Regional nodes not assessed   | No   |
| N0         |     | None  | No   |
| N1         |     | 1 tumor-involved node<br><b>or</b> in-transit, satellite and/or microsatellite metastases without tumor-involved nodes  |  |
|            | N1a | 1 clinically occult   | No   |
|            | N1b | 1 clinically detected   | No   |
|            | N1c | None  | Yes  |
| N2         |     | 2 or 3 tumor-involved nodes<br><b>or</b> in-transit, satellite and/or microsatellite metastases with 1 tumor-involved nodes   |  |
|            | N2a | 2 or 3 clinically occult  | No   |
|            | N2b | 2 or 3 (min. 1 clinically detected)   | No   |
|            | N2c | 1 clinically occult or detected   | Yes  |
| N3         |     | 4 or more tumor-involved nodes<br><b>or</b> in-transit, satellite and/or microsatellite metastases with 2 or more tumor-involved nodes<br><b>or</b> any number of matted nodes with or without in-transit, satellite and/or microsatellite metastases |  |
|            | N3a | 4 or more clinically occult   | No   |
|            | N3b | 4 or more (min. 1 clinically detected)<br>or any number of matted nodes   | No   |
|            | N3c | 2 or more (clinically occult or detected<br>and/or any number of matted nodes)  | Yes  |

| M category   |        | Anatomic site   | Lactate dehydrogenase serum level |
|--------------|--------|---|-----------------------------------|
| M0           |        | No evidence of distant metastasis   | Not applicable                    |
| M1           |        | Evidence of distant metastasis  | See below                         |
|              | M1a    | Distant metastasis to skin, soft tissue including muscle and/or non-regional lymph node                         | Not recorded or unspecified       |
|              |        |   | Not elevated (0)                  |
|              | M1b    | Distant metastasis to lung with or without M1a sites of disease   | Elevated (1)                      |
|              |        |   | Not recorded or unspecified       |
|              | M1c    | Distant metastasis to non-central nervous system (CNS) visceral sites with or without M1a or b sites of disease | Not elevated (0)                  |
|              |        |   | Not recorded or unspecified       |
|              | M1d    | Distant metastasis to CNS with or without M1a, b or c sites of disease  | Elevated (1)                      |
|              |        |   | Not recorded or unspecified       |
|              | M1a(0) |   | Not elevated (0)                  |
|              |        |   | Elevated (1)                      |
|              | M1a(1) |   | Not elevated (0)                  |
| Elevated (1) |        |   |                                   |
| M1b(0)       |        | Not elevated (0)  |                                   |
|              |        | Elevated (1)  |                                   |
| M1b(1)       |        | Not elevated (0)  |                                   |
|              |        | Elevated (1)  |                                   |
| M1c(0)       |        | Not elevated (0)  |                                   |
|              |        | Elevated (1)  |                                   |
| M1c(1)       |        | Not elevated (0)  |                                   |
|              |        | Elevated (1)  |                                   |
| M1d(0)       |        | Not elevated (0)  |                                   |
|              |        | Elevated (1)  |                                   |
| M1d(1)       |        | Not elevated (0)  |                                   |
|              |        | Elevated (1)  |                                   |

Table 2 – Melanoma TNM classification according to the 8<sup>th</sup> edition AJCC staging system (Amin 2017)

### 1.3.2. Non-melanoma skin cancers

#### 1.3.2.1. Basal cell carcinoma

In 2019, The European Association of Dermato-Oncology (EADO) proposed a new dichotomic classification for BCC, more pragmatic and operational. “Easy-to-treat” BCC category includes 95% of cases, easy to manage with standard surgery or alternative destructive treatments. “Difficult-to-treat” BCC category includes all locally advanced or metastatic BCCs but also common BCCs with specific management issues: surgical difficulty to maintain functional or aesthetic features due to the size and/or localization of the lesion, poorly defined limits of the lesion, multiple prior recurrences, patient’s comorbidities, and more aggressive histological subtypes such as plexiform or metatypical BCC (Peris 2019).

#### 1.3.2.2. Cutaneous squamous cell carcinoma

Staging for cSCC is based on a conventional TNM classification. Several systems exist with specific classification for head and neck cSCCs (Stratigos<sup>2</sup> 2020). AJCC/Union for international cancer control (UICC) TNM staging system is the most popular classification (table 3).

|                   |   |  |  |
|-------------------|---|--|--|
| <b>Tumor</b>      | Tx  | Primary tumor cannot be assessed   |  |
|                   | T0  | No evidence of primary tumor   |  |
|                   | Tis   | Carcinoma in situ  |  |
|                   | T1  | Greatest dimension up to 2cm   |  |
|                   | T2  | Greatest tumor dimension > 2cm but < 4cm   |  |
|                   | T3  | Greatest dimension of tumor ≥ 4cm or minimal erosion of the bone or perineural invasion or deep invasion   |  |
|                   | T4  | Tumor with extensive cortical or medullary bone involvement (T4a), invasion of the base of the cranium or invasion through the foramen of the base of the cranium (T4b)                          |  |
| <b>Node</b>       | Nx  | Regional lymph nodes cannot be assessed  |  |
|                   | N0  | No regional lymph node metastasis  |  |
|                   | N1  | Metastasis in a single ipsilateral lymph node, 3cm or less in greatest dimension   |  |
|                   | N2  | Metastasis in a single ipsilateral lymph node, more than 3cm but not more than 6cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6cm in greatest dimension |  |
|                   |   | N2a  | Metastasis in a single ipsilateral lymph node, more than 3cm but not more than 6cm in greatest dimension |
|                   | N2b   | Metastasis in multiple ipsilateral lymph nodes, none more than 6cm in greatest dimension   |  |
|                   | N2c   | Metastasis in bilateral or contralateral lymph nodes, none more than 6cm in greatest dimension   |  |
| N3                | Metastasis in a lymph node, more than 6cm in greatest dimension |  |  |
| <b>Metastasis</b> | M0  | No distant metastasis  |  |
|                   | M1  | Distant metastasis   |  |

Table 3 - cSCC TNM classification according to the 8<sup>th</sup> edition AJCC/UICC staging system (Amin 2017)

## 1.4. Prognosis of skin cancers

### 1.4.1. Melanoma

The stage grouping combines the T, N and M subclassifications into categories with a similar prognosis (table 4).

| Clinical stage group | T     | N     | M  |
|----------------------|-------|-------|----|
| 0                    | Tis   | N0    | M0 |
| IA                   | T1a   | N0    | M0 |
| IB                   | T1b   | N0    | M0 |
|                      | T2a   | N0    | M0 |
| IIA                  | T2b   | N0    | M0 |
|                      | T3a   | N0    | M0 |
| IIB                  | T3b   | N0    | M0 |
|                      | T4a   | N0    | M0 |
| IIC                  | T4b   | N0    | M0 |
| III                  | Any T | ≥ N1  | M0 |
| IV                   | Any T | Any N | M1 |

| Pathological stage III subgroups | T           | N                     | M  |
|----------------------------------|-------------|-----------------------|----|
| IIIA                             | T1a/b – T2a | N1a or N2a            | M0 |
|                                  | T0          | N1b, N1c              | M0 |
| IIIB                             | T1a/b – T2a | N1b/c or N2b          | M0 |
|                                  | T2b/T3a     | N1a – N2b             | M0 |
| IIIC                             | T0          | N2b, N2c, N3b, or N3c | M0 |
|                                  | T1a – T3a   | N2c or N3a/b/c        | M0 |
|                                  | T3b/T4a     | Any N ≥ N1            | M0 |
|                                  | T4b         | N1a – N2c             | M0 |
| IIID                             | T4b         | N3a/b/c               | M0 |

Table 4 – Stage groups according to the 8<sup>th</sup> edition AJCC staging system (Amin 2017)

The survival rates by stage are illustrated in figure 19 (Keung 2018). In Belgium, the 5-year survival rate for a man with melanoma is 94.2% and for a woman 97.3%, all stages combined (Belgian Cancer Registry Group 2022).

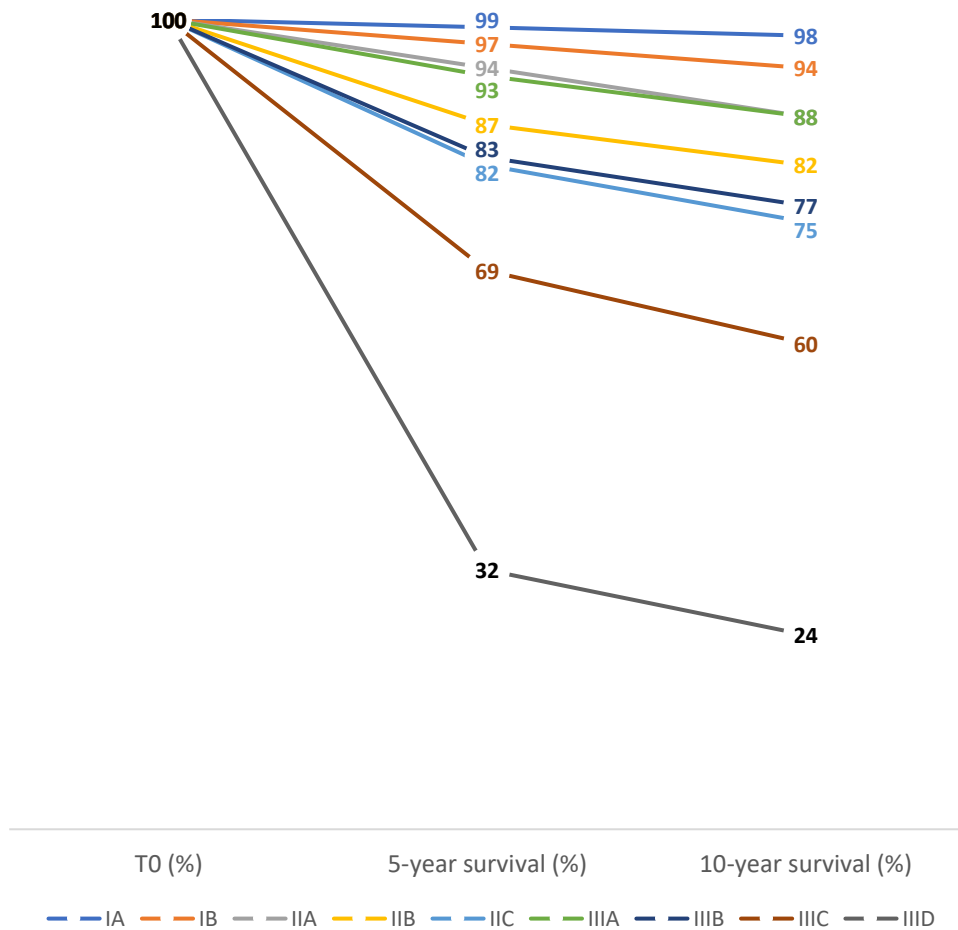


Figure 19 – Kaplan-Meier curves for melanoma-specific survival at 5 and 10 years according to the stage (Keung 2018)

## 1.4.2. Non-melanoma skin cancers

### 1.4.2.1. Basal cell carcinoma

BCC is the skin cancer with the highest survival rate without significant decline compared to the general population. In the very rare cases of advanced BCC, overall survival is shortened (Peris 2019).



### 1.4.2.2. Cutaneous squamous cell carcinoma

In most cases, cSCCs are indolent tumors. With early and appropriate therapeutic management, the 5-year survival rate is over 90%. According to several cohort study, recurrence was reported in less than 5% of cases, mainly as locoregional relapse. On the other hand, recent studies have shown worse outcomes for cSCC in immunosuppressed patients. In this specific group, metastatic status was estimated at least doubled and survival after nodal involvement is significantly reduced, with a 5-year survival rate estimated at 55% for these advanced cSCCs. Patients with significant field cancerization are also at increased risk (Stratigos<sup>2</sup> 2020).

## 1.5. Treatment of skin cancers

### 1.5.1. Melanoma

The therapeutic strategy for melanoma is complex and should ideally be determined by a multidisciplinary skin cancer board. For each patient, the following information is required: accurate clinical history, thorough examination, histopathological tumor report and clinical staging.

Figure 20 summarizes the range of treatment options based on the TNM classification (Garbe<sup>1</sup> 2022).

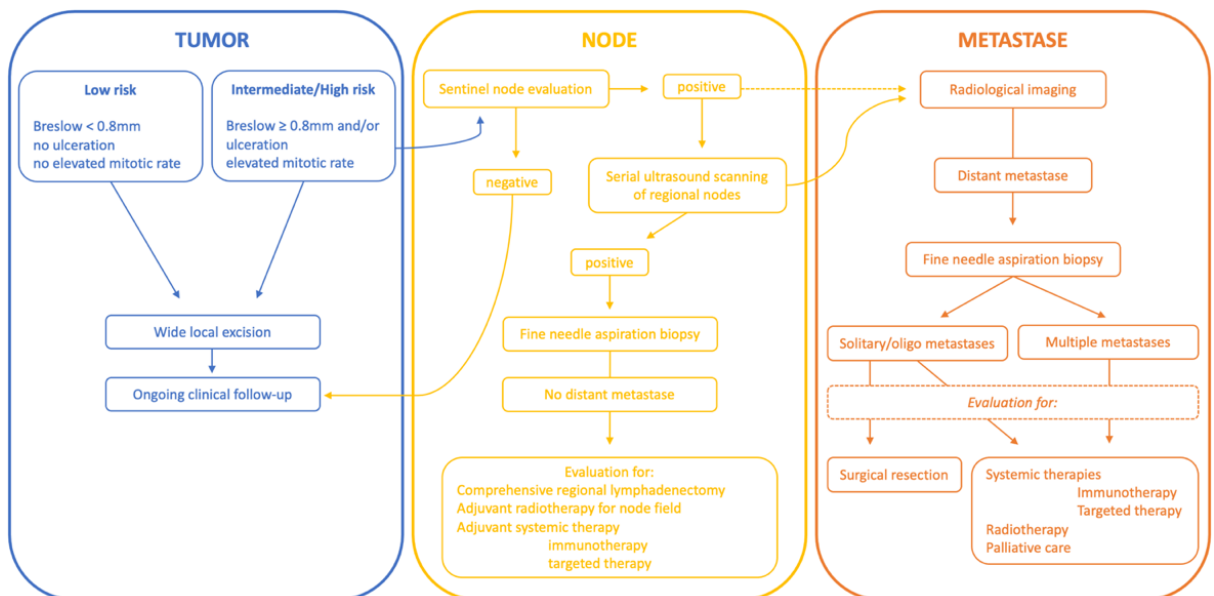


Figure 20 – Melanoma care management according to TNM classification (Garbe<sup>1</sup> 2022)

## 1.5.2. *Non-melanoma skin cancers*

### 1.5.2.1. Basal cell carcinoma

Surgery remains the gold standard treatment for “easy-to-treat” BCCs, although alternative destructive options have been developed (topical imiquimod, topical 5-fluorouracil, photodynamic therapy, topical methotrexate, ...) (Peris 2019, Lebas 2019).

Regarding “difficult-to-treat” BCCs, treatment is highly complex and therapeutic strategy plan from multidisciplinary skin cancer board is highly recommended. For these advanced lesions, standard therapy has always been surgery and/or radiotherapy but these options not always suit all medical situations. The first systemic therapy was hedgehog inhibitors (HHI). HHIs result in stabilization of disease progression or even regression of tumor volume, which is particularly interesting in a neoadjuvant setting for tumor debulking prior to surgery. However, up to 50% of patients experience considerable side effects (dysgeusia, fatigue, muscle pain and alopecia). Moreover, primary or secondary resistance to HHIs exists. Recently, phase III pivotal studies with programmed cell death protein-1 (PD-1) inhibitors were conducted. Cemiplimab was the first PD-1 inhibitor that received Food and Drug Administration (FDA) approval for the treatment of locally advanced BCC after failure of HHI (Damsin<sup>1</sup> 2022).

### 1.5.2.2. Cutaneous squamous cell carcinoma

The majority of cSCCs is easily managed by surgery without any adjuvant treatment. In contrast, locally advanced cSCCs (lacSCC) and metastatic cSCCs (mcSCC) require a staging workup and a personalized therapeutic approach established by a multidisciplinary team. Conventional management is based on surgery and/or radiotherapy. For cases judged as inoperable, multiple therapeutic options should be considered: intralesional chemotherapy, electrochemotherapy, systemic chemotherapy or targeted therapies. Before 2018, targeted therapies for cSCCs included erlotinib and cetuximab, both with very modest response rates. In 2018, the FDA approved cemiplimab for lacSCC/mcSCC management. PD-1 inhibitors demonstrated higher response rates in comparison with previous conventional therapies (Lebas 2021).

## 1.6. Prevention of skin cancers

The World Health Organization (WHO) defines prevention as “approaches and activities aimed at reducing the likelihood that a disease or disorder will affect an individual, interrupting or slowing the progress of the disorder or reducing disability” (World Health Organization 2005).

There are three different levels of prevention. Primary prevention brings together actions designed to reduce the risk to develop a health problem. Secondary prevention aims to diagnose a health problem as quickly as possible to limit its development. Tertiary prevention applies to diseases that have already been contracted and seeks to limit the occurrence of complications and recurrences (World Health Organization 2005). These three levels of prevention also apply to skin cancers.

### 1.6.1. Primary prevention of skin cancers

Primary prevention of skin cancers mainly involves limiting exposure to modifiable risk factors. These have already been defined above. Thus, the scope of primary prevention of skin cancers is limited to modifying exposure to UV radiation. The strategies implemented can be divided into two main areas: specific UV protection measures and interventional strategies (Perez 2022).

#### 1.6.1.1. Specific UV protection measures

Three ways of specific UV protection measures are described.

Physical protection from natural or artificial UV radiation simply involves limiting or avoiding exposure and using protective clothing and accessories. For the latter, wearing dark clothing covering the most frequently exposed parts of the body is recommended, as well as hats and sunglasses. There is a scale of UV protection for fabrics called "UV Protection Factor" (UPF) to assess the photoprotective factor of a textile item (Gefeller 2018).

Topical protection is mainly provided by sunscreens. Although sunscreens are regularly the subject of controversy, their regular use has been shown to have a significant impact on reducing the risk of skin cancer (Waldman 2019). The consensus is to apply a waterproof, broad-spectrum sunscreen with a high sun protection factor (SPF), 15-20 minutes before sun exposure and reapply every two hours (Division of Cancer Prevention and Control 2023).

Systemic protection is based on the hypothesis of oxidative stress induced by UV exposure. Several systemic antioxidants have been proposed as alternative or additional methods of photoprotection. However, the FDA has ruled on these supplements and warned that they do not respond to required safety and efficacy standards (Gottlieb 2018). Used in specific situations, systemic chemoprevention

using nonsteroidal anti-inflammatory drugs or retinoids has demonstrated a moderate benefit but requires more extensive clinical trials (Parrado 2018).

### 1.6.1.2. Interventional strategies

Educational intervention can play a critical role in primary prevention. Opportunities for UV exposure are occurring at an increasingly early age. These campaigns use the mass media to convey simple but powerful messages about protection against UV exposure. Educational activities are also organized in schools and workplaces (Perez 2022). One of the most popular campaigns is the "SunSmart" campaign set up by the Australian government (Iannacone 2014). In Belgium, primary prevention campaigns are largely run by two institutions: the national cancer organization "Fondation contre le cancer" and the European non-profit association "Euromelanoma". For its 24<sup>th</sup> campaign in 2023 with the slogan "Do you use protection?", Euromelanoma has focused on two graphic projects: a leaflet covering the key aspects of primary prevention of skin cancer (figure 21), and a comic strip to reach a younger audience. Although these educational interventions remain important in terms of health promotion, their impact on the incidence of skin cancer appears to be limited (Køster 2018).



Figure 21 – Euromelanoma 24th campaign “Do you use protection?” leaflet (“clj8ksapy1v1ohjpp0mz9ihy-euromelanoma-2023-campaign-leaflet-final-print-ready-page-1” on [Euromelanoma.eu](http://Euromelanoma.eu) website consulted on 19.09.2023)

Behavioral interventions consider biological, behavioral, cognitive, emotional, social, and environmental factors in designing prevention strategies. So, focusing on the damage caused by UV exposure in terms of skin ageing may have more impact than focusing the message on the risk of skin cancer (Persson 2018).

## 1.6.2. Secondary prevention of skin cancers

Secondary prevention of skin cancer involves early detection and prompt initiation of appropriate treatment. There are two main aspects to this approach: skin cancer screening and chemoprevention (Rojas 2022).

### 1.6.2.1. Skin cancer screening

Screening refers to the detection of a disease at an asymptomatic stage. Thus, for a given disease, screening is recommended on following conditions: the disease represents a public health problem, the epidemiology has been clearly studied, an asymptomatic phase is detectable, and a target population has been defined. In addition, three levels of screening are described. Mass screening concerns the whole population without considering risk factors. Selective screening considers risk factors and selects a population to screen. Opportunistic screening occurs at an individual level (Speechley 2017).

Skin self-examination (SSE) is a screening method performed by patients themselves. A commonly accepted fact is that more than half of melanoma are detected by the patient himself (Avilés-Izquierdo 2016). Through mass screening campaigns (figure 22) or individual education, learning a simple, systematic method of SSE based on the ABCDE criteria (described above) or the ugly duckling sign (defined as a skin lesion looking different from others) can be a useful tool (Rojas 2022).

The infographic is divided into several sections. On the left, a photo shows a doctor examining a patient's skin. The main title is 'Four main types of suspicious skin lesion'. Below this are four columns, each with a number and a type of skin cancer: 1. Melanoma, 2. Basal cell carcinoma, 3. Squamous cell carcinoma, and 4. Actinic keratosis. Each column includes a small image of the lesion and a brief description. To the right of these columns is a section titled 'The 'ABCDE' rule' which lists five criteria: A (Asymmetry), B (Border), C (Colour), D (Diameter), and E (Evolution). Below this is an illustration of a hand holding a magnifying glass over a skin lesion, with the text 'The 'Ugly Duckling' sign' and a description of it. On the far right, a section titled 'How to check your skin' provides instructions on when and how to perform a skin self-examination, including a list of 7 steps. At the bottom right, there is a small icon of a person with a speech bubble and a first aid symbol.

Figure 22 – Euromelanoma 24th campaign “Do you use protection?” leaflet (“cloud5np20k0e6hjpgdnbhc7u6-euromelanoma-2023-campaign-leaflet-final-print-ready-2” on [Euromelanoma.eu](http://Euromelanoma.eu) website consulted on 19.09.2023)

Total body examination (TBE) performed by healthcare providers represents the second level of skin cancer screening. Only one in four TBE is carried out in a PHC, the majority being performed directly by dermatologists (Ferris 2017). TBE can be improved using non-invasive imaging techniques, especially dermoscopy. The evidence of the use of TBE as a mass screening tool is variable. The European consensus-based interdisciplinary guidelines recommend a selective screening for patients with high risk of skin cancer (nevroid basal cell carcinoma syndrome, first-degree relatives of melanoma patient, immunocompromised patient, ...) (Peris 2019, Garbe<sup>1</sup> 2022).

#### 1.6.2.2. Chemoprevention

The use of topical or systemic agent to prevent the progression or recurrence of skin cancer in patients with an history of pre-malignant or malignant skin lesions is the second aspect of secondary prevention. The most concrete example is the use of oral acitretin (10mg t.i.w. to 25mg q.d.) in OTR for the secondary prevention of AK and cSCC (Nemer 2019).

#### 1.6.3. *Tertiary prevention of skin cancers*

Tertiary prevention covers all strategies aimed to prevent progression, detect recurrence, maintain health-related quality of life, and reduce complications in patients with symptomatic or advanced skin cancer (Rojas 2022).

##### 1.6.3.1. Surveillance

Follow-up visits with a healthcare provider are the cornerstone of surveillance. Their time interval is variable, depending on the characteristics of the skin cancer, the risk of recurrence and the time after diagnosis (table 5). These follow-up recommendations meet level IV evidence, corresponding to evidence from expert committee reports or opinions and/or clinical experience of respected authorities, being the lowest level of evidence available. Other strategies are also included in this surveillance, such as SSE (Rojas 2022).

| Skin cancer type | Tumor characteristics               | TBE interval time   | Level of evidence |
|------------------|-------------------------------------|---|-------------------|
| BCC              | Recurrent or multiple BCC           | Year 1-5: 6-12 months   | IV                |
| cSCC             | Low-risk primary cSCC               | Year 1-5: 6-12 months   | IV                |
|                  | High-risk primary cSCC              | Year 1-2: 3-6 months<br>Year 3-5: 6-12 months<br>Year 6+: 12 months |                   |
|                  | Locally advanced or metastatic cSCC | Year 1-5: 3 months<br>Year 5+: 6-12 months                          |                   |
| Melanoma         | Stage IA                            | Year 1-3: 6 months<br>Year 4+: 12 months                            | IV                |
|                  | Stage IB-IIB                        | Year 1-3: 3-6 months<br>Year 4-10: 6 months<br>Year 10+: 12 months  |                   |
|                  | Stage IIC-IIIC                      | Year 1-3: 3 months<br>Year 4-10: 6 months<br>Year 10+: 12 months    |                   |
|                  | Stage IIID                          | Year 1-3: 3 months<br>Year 4-10: 6 months<br>Year 10+: 12 months    |                   |
|                  | Stage IV                            | Year 1-3: 3 months<br>Year 4-10: 6 months<br>Year 10+: 12 months    |                   |

Table 5 – Risk-adapted follow-up European recommendations (adapted from Rojas 2022)

### 1.6.3.2. Educational intervention

At the tertiary prevention phase, educational intervention aims to reduce risky behavior related to UV exposure and to promote SSE (Rojas 2022). Indeed, although most skin cancer patients adopt a responsible attitude to UV exposure and perform regular SSE, some studies shown that a substantial proportion (up to 25%) of these patients do not yet comply with these recommendations (Mayer 2012, Failla 2012).

### 1.6.3.3. Therapeutic intervention

Depending on how tertiary prevention is defined, some therapeutic interventions can be considered as tertiary preventive strategies (Rojas 2022).

## 2. Tele dermatology

### 2.1. History of telemedicine

Telemedicine (TM) is based on telecommunication technologies to connect healthcare workers and patients, sharing clinical information.

The beginnings of TM go back to the early 1900s when radio was used by ship captains to receive medical guidance (Wootton 2001). Television represented an evolving attempt for the transmission of visual data with high reproducibility (Vidmar 1999). The prototype required however expensive equipment and highly trained technicians, hence limiting the use of TM rather as a research tool rather than applicable for the daily medical practice. In the beginning of the 1980s, the new codification of images into an electronic binary code permitted the first trials of digital video teleconferencing (Vidmar 1999). Recently, the rapid and increasing development of the widespread internet provided the first experiences of the store-and-forward (S&F) modality (described below) for TM.

Today, mobile technologies represent a major advance in TM, both in terms of technical performances, availability, user-friendliness, and low cost permitting easy access to TM for most of the population and healthcare providers (Coates<sup>1</sup> 2014).

### 2.2. Definition of tele dermatology

Tele dermatology (TD) is defined as the practice of dermatological care at distance using imaging devices and telecommunication technologies. The first reports in the literature date from the early 1990s (Vorland 1992). Later, the use of TD was described in 1993 based on experiences in Norway, with a very low-density population and a restricted number of dermatologists (Rinde 1993).

### 2.3. Development of tele dermatology

TD references in the literature are increasing steadily over the last 20 years. Indeed, the impact of TD is significant in the daily dermatology practice, explained by various factors.

The prevalence of skin diseases exceeds that of excess weight, high blood pressure and oncologic diseases. This has the potential to be a significant reason for consultation (Bickers 2006). In the US, dermatological issues account for 12.4% of primary healthcare visits (Verhoeven 2008). In France, dermatological issues represent 6% of overall consultations (Letrilliart 2014). The most reported dermatological diseases categories are atopic dermatitis and other allergic manifestations (18.9%), infectious rashes (13.8%), cutaneous tumors (12.8%) and fungal infections (10.4%) (Bureaux 2012). Moreover, a specialized advice is requested by FHP in 30% of cases, up to 76% of cases about skin tumor diagnosis (Mathis 2019).



This proportion of referral request is significantly higher than the mean rate of specialized advice requests for overall primary care consultations, estimated at 5% (Labarthe 2004). The main reason for requesting a specialist opinion is diagnostic uncertainty (Bureaux 2012). Based on ten clinical cases covering diagnostic and therapeutic questions, a study conducted in 2020 showed an average score of 59.5/100, reflecting a lower level of dermatological knowledge in PHC compared to other specialty knowledge (Damas 2020). Outside Europe, an Australian publication demonstrated a concordance rate between FHPs and dermatologists at 45% (Tran 2005). The Belgian situation appears to be comparable, although there are no official figures to support it.

In the US, although the number of dermatologists is increasing every year, the average time for a face-to-face (FTF) visit is increasing, reflecting a relative shortage of specialists (Yoo 2010, Kimball 2008). Curiously, this period is reduced by half for cosmetic requests (Resneck 2007). Moreover, currently the younger dermatologists tend to shorten their workweek, exacerbating the shortage of dermatology services (Kimball 2008). In France, the epidemiological situation seems to be of greater concern. The median waiting time for a FTF appointment with a dermatologist is estimated at 61 days. This delay is judged too long by both patients and referring clinicians (Carnot 2019). Moreover, projections for 2030 are particularly unfavorable for dermatology: the decrease in the total number of dermatologists is estimated at 32%. This would reinforce the shortage by a relative decrease of available dermatologists (Bureaux 2012).

Finally, the relative difficulty of access to specialized medicine can also be explained by the geographical distance separating the patient from a secondary or tertiary healthcare center (Coates<sup>1</sup> 2014).

In summary, the burden of skin diseases, the relative lack of dermatological knowledge of the FHP, the delay for a FTF appointment with dermatologists and the geographical distance from specialized care centers are all factors that led to the development of TD. Figure 23 illustrates these rationales.

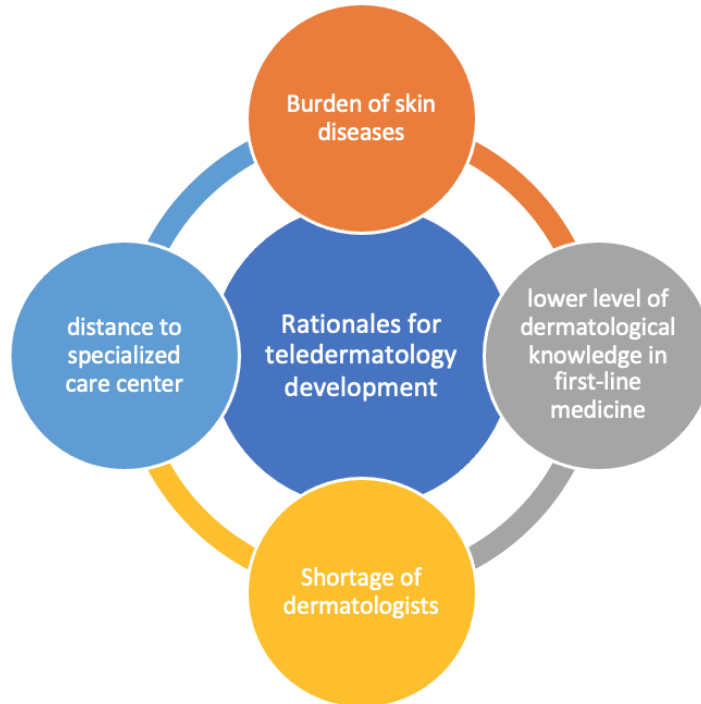


Figure 23 - rationales for tele dermatology development

#### 2.4. Acceptance of tele dermatology

For increasing the acceptance of TD, it had to prove its reliability and accuracy. Reliability refers to agreement or reproducibility of a diagnostic assessment, introducing the concept of complete (same single diagnosis for all consultants) versus partial (list of several diagnoses) agreement. Accuracy reflects whether diagnoses reached are correct or not and is assessed with gold standard comparator, histopathology. In the literature, publications about this topic can be divided in four axes: diagnostic agreement between tele dermatologists and FTF dermatologists, intragroup diagnostic agreement, diagnostic accuracy, and management plan agreements.

In terms of diagnostic agreement between tele dermatologist and FTF dermatologists, global complete agreement rates were 41% to 94% and partial agreement rates were 50% to 100% (Levin 2009).

Moreover, some studies detailed the level of agreement within tele dermatologists themselves in comparison with FTF dermatologist visits. Among all studies, tele dermatologists demonstrated a complete intragroup agreement in 46% to 83% and a partial intragroup agreement in 84% to 92%. FTF dermatologists demonstrated a complete intragroup agreement in 54% to 95% and a partial intragroup agreement in 90% to 100% (Levin 2009).

Diagnostic accuracy is critical, especially for neoplasms. Data are developed in the “Teledermoscopy” section. Indeed, the combination of dermoscopy with TD had a significant impact in diagnostic accuracy regarding cutaneous neoplasms telediagnosis (Levin 2009).

Appropriateness of recommended clinical management represents the most important aspect to evaluate in TD. However, it is difficult to establish a single definition of this concept and to exclude the influence of many factors, thus limiting the number of studies that have evaluated this topic. Investigators indicated that intergroup or intragroup disagreements mostly reflected differences in management habits (Levin 2009).

Two main modalities of teledermatology have been described. The store-and-forward (S&F) modality with an asynchronous operation and real-time (RT) modality with a live video connexion. Details are described in the “Materials and methods of Teledermatology” section. Both S&F and RT modalities reach high degrees of complete agreement and even a higher degree of partial agreement (Jiang 2022). In comparison with S&F modality, hybrid modality (S&F and RT combination) does not appear to be more reliable (Brinker 2018). Many studies support the high diagnostic accuracy of S&F modality confirmed by a subsequent histopathology report (Edison 2008, Warshaw 2011). Despite these efficiency data, it should be noticed that diagnostic accuracy of a FTF visit is reportedly 11% higher than a TD consultation (Warshaw 2011).

Three types of users in TD were identified: patient, referring clinician and teledermatologist. The satisfaction of these three groups was assessed.

In terms of patient satisfaction, many studies show a level of satisfaction comparable to FTF visits, reaching 74% to 93% (Collins 2004, Whited 2015). Reported positive features included reduction of the waiting time, easy access to specialized care, confidence about data processing and privacy (Hsueh 2012, Santiago 2023, Lopez-Liria 2022). Reported negative features concerned the following items: altered patient-provider therapeutic relationship, incomplete transmission of information as well as appropriate treatment and follow-up (Withed 2015).

For the referring clinicians, positive experiences were substantially higher with S&F modality than with RT modality (Withed 2015), RT consultations were reported more time-consuming. Referring clinician satisfaction rates ranged from 63% to 92%.

In terms of teledermatologist satisfaction, most dermatologists involved in a TD program claim to provide care quality similar to FTF care (Edison 2013, Mounessa 2017).

## 2.5. Tele dermatology today

Data from the WHO eHealth survey shows an increasing implementation of TD systems. In 2009, a TD service was established in only 16% of 114 responding countries. A 2015 updated review noticed a TD service, from pilot projects to well-established systems, in 46% of 125 responding countries. Most TD programs are active in America and Europe (McKoy 2021). In Europe, the willingness to develop TD programs appears to be related to the organizational modalities of national healthcare systems and the ratio of dermatologists to population. Three European countries stand out for their advanced tele dermatology programs: the Netherlands, the United Kingdom and Spain (van der Heijden<sup>1</sup> 2010, Mehrtens 2019, Romero 2018).

In addition, TD has emerged as a critical tool of delivering primary and/or consecutive care remotely to patients during the COVID-19 pandemic. All the three TD modalities were exploited, with a preference for RT modality. The triage model allowed an effective selection of patients requiring a FTF visit, minimizing the risk of COVID-19 transmission (Loh 2021). While TD is again less used today compared to FTF visits, the COVID-19 pandemic certainly had a positive impact on the perception of TD by novice users (Silva 2021).

In Belgium, the TM situation is much less advanced in comparison with neighboring countries (Nunes de Sousa 2021), probably linked to the relative high ratio of specialist per capita and as the mean distance to a specialized care center is not so high. Still, patients complain about long waiting times. In the field of TD, before 2020, only non-governmental pilot projects were developed in collaboration with university dermatology centers (Damsin 2019, Kips 2019). In 2021, the first TD pilot project funded by the Belgian national healthcare system was initiated. This study was based on a consultative model in a S&F modality. The aim of this pilot study was to assess the feasibility, reliability, speed, accessibility, safety, cost-effectiveness, privacy and policy of dermatological recommendations via remote consultations. In less than a year, 2000 S&F advices have been registered. The conclusions of the National Institute for Health and Disability Insurance confirm the acceptability and satisfaction of all three involved parties (patients, FHPs, and dermatologists). Based on the findings and recommendations of this pilot project, the federal public body of social security is currently developing a broader framework for TM integrating medical, technical, and legal considerations (Heselmans 2022).

The situation of TD in developing countries is even more contrasting than in developed countries. In sub-Saharan Africa, while only 14% of the countries have trained dermatologists or dermatopathologists, skin complaints account for up to 24% of primary healthcare consultations (Tsang 2010). The development of S&F modality in TD has been one of the responses to reduce the burden of skin diseases and improve diagnostic performance of PHCs (Colven 2011, Frühauf 2013). However, these projects face specific challenges in developing countries: patient illiteracy, lower follow-up adherence, drug shortage, limited internet access, ... (Chang 2011).

## 2.6. Materials and methods of teledermatology

### 2.6.1. *Teledermatology modalities*

Three distinct TD modalities have been developed to accommodate different clinical situations, according to the referring providers' abilities, teleconsultants' practice organization, and primary healthcare system infrastructures (Johnson 2011). Figure 24 compares the two main modalities of TD.

#### 2.6.1.1. Store-and-forward modality

S&F modality is based on an asynchronous access to data by consultants. It interferes less with the daily workflow and is more efficient for healthcare providers practicing across time zones. However, S&F modality may require multiple acquisitions if clinical data are missing, or in the event of non-adequate image acquisitions. Moreover, for educational aspect, the S&F modality seems less suitable (Johnson 2011).

#### 2.6.1.2. Real-time modality

RT modality is based on a direct interaction using a live video connection between the healthcare provider and the dermatologist. RT modality compels coordination between both consultants and requires a significant bandwidth, currently not considered anymore as an obstacle. RT modality allows a more efficient case history by clarifying consultant's questions in vivo. It also allows in vivo adaptation of images of the patient. Moreover, RT modality offers better educational opportunities (Johnson 2011).

#### 2.6.1.3. Hybrid modality

The hybrid modality is the latest developed modality in TD. It combines the advantageous aspects of both S&F and RT modalities (Johnson 2011).

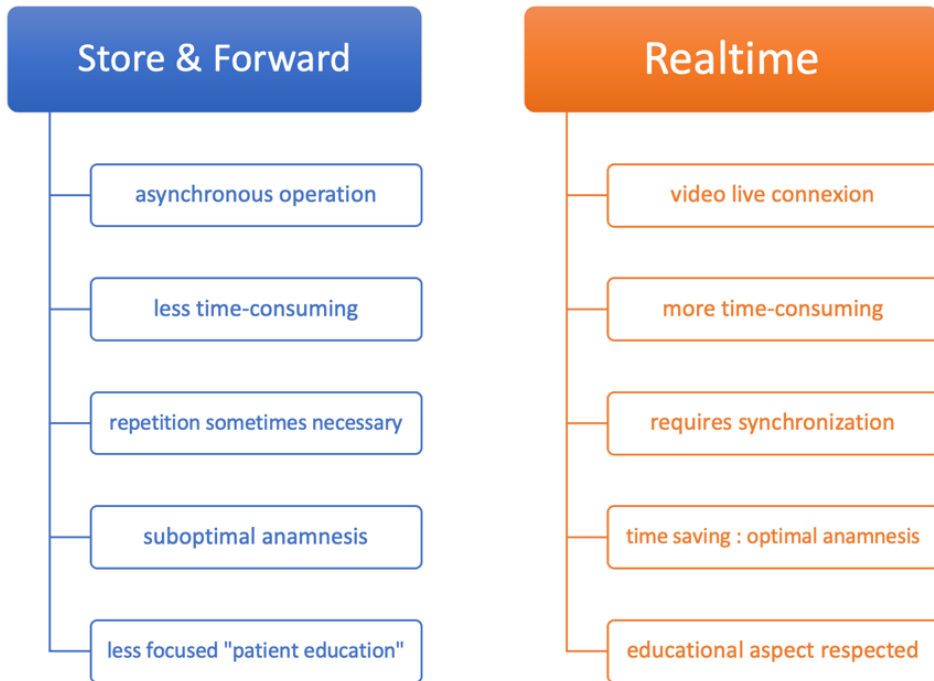


Figure 24 - Comparison between S&F and RT modalities

### 2.6.2. Practice models

Four TD practice models have been described: consultative, triage, direct care, and follow-up. Once again, each practice model answers to different variables: referring providers' abilities, teleconsultants' practice organization, primary healthcare system infrastructures, ... (Pathipati 2011). Figure 25 resumes practice models in TD.

#### 2.6.2.1. Consultative model

The consultative model is the most commonly and widely used system. It can be applied to all the TD modalities. Teledermatologists provide recommendations to referring providers who assume the responsibility to apply or not these recommendations (Pathipati 2011).

#### 2.6.2.2. Triage model

The purpose of the triage model is the prioritization of the patient care pathway. By determining the need for a FTF dermatology visit, the triage model may improve access to specialized care by reducing unnecessary referrals (Pathipati 2011).

### 2.6.2.3. Direct care model

The direct care model establishes a direct communication between dermatologists and patients. This model attempts to be as close as possible to a FTF visit. However, the dermatologist's unwillingness to prescribe medications to patients not seen in clinic settings represents a major limiting factor for this approach (Pathipati 2011).

### 2.6.2.4. Follow-up model

The follow-up model is a variant of the direct care model. It is dedicated to the long-term monitoring of chronic skin conditions. Indeed, some clinical situations require frequent clinic visits to assess disease activity and optimize treatment and could hence benefit from TD. Follow-up TD sessions may save time for dermatologists, and travel time and money for patients (Pathipati 2011).

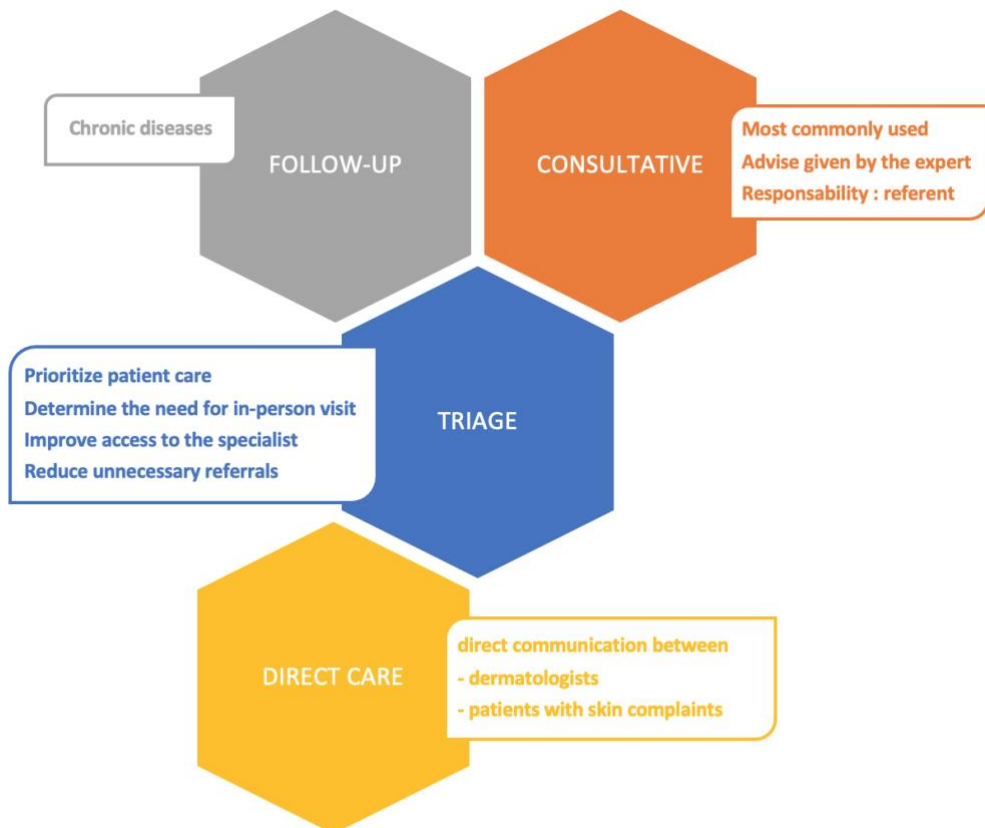


Figure 25 - Features of TD models

### *2.6.3. Mobile teledermatology*

The ever-evolving mobile internet technologies continuously increase the possibilities and usefulness of TM. In 2022, 62.5% of the world's population had access to mobile internet (Ceci 2023). The smartphones represent a highly interesting tool for interconnecting across social, technological, and medical dimensions (Coates<sup>1</sup> 2015).

By the miniaturization and empowerment of telecommunication devices, mobile TD allows patients to play an active role. For example, the patient can bypass the FHP and be connected directly with the teledermatologist. This approach has been of particular interest in the field of chronic skin conditions (Balato 2013, Koller 2011). On the providers side, computer screens or handheld tablets were found to be more effective to assess images (Brandt 2012).

In addition, increasing mobile phone users in developing countries can be a solution to some of the challenges mentioned above (Frühauf 2013).

### *2.6.4. Teledermoscopy*

The benefit of dermoscopy for increasing the diagnostic accuracy of a tumor lesion compared to “naked eye” examination has been mentioned above.

Combined with TD, this imaging technology enhances performance in remote skin cancer screening with high sensitivity and specificity rates. The diagnostic accuracy of teledermoscopy (TDS) was reported increased by 15% (absolute difference) compared to macroscopic images alone (Warshaw 2011).

It was also critical to compare TDS to FTF dermoscopy. In fact, no significant difference in sensitivity was observed between FTF consultations and TDS referrals, especially concerning triage of benign versus malignant lesions. TDS triage sensitivity was 85.7% and FTF triage sensitivity was 88.2%, with no statistically significant difference. Regarding triage specificity, higher scores were observed with FTF (85.9%) in comparison with TDS (75.8%), but without statistically significant difference. The only statistically significant difference was diagnostic accuracy for primary diagnosis: 58.2% for TDS and 70.9% for FTF (Vestergaard<sup>1</sup> 2020). From a clinical perspective, triage of benign versus malignant lesion seems more relevant than the primary diagnosis. Indeed, the main objective remains to speed up the management of suspicious lesions (van Sinderen 2022, Vestergaard<sup>1</sup> 2020).

The implementation of dermoscopy devices directly attached to a smartphone enables to combine mobile TD and TDS (Börve 2015). However, the cost of materials and the necessity of learning the basics of dermoscopic analysis may limit a more widespread use of TDS (Coates<sup>2</sup> 2015).



Finally, the acceptance of patients with TDS referrals was investigated. In general, almost 90% of patients were satisfied or neutral with TDS referrals in comparison with conventional FTF visits. The reduction in waiting time seems to be the most important factor in favor of TDS referrals, especially in this field of onco-dermatology. The reported main concern was the therapeutic management in case of malignant lesions (Gillins 2020).

#### *2.6.5. Teledermatology as an educational tool*

The educational scope of TD should be highlighted.

Without making it a primary outcome, any TD project facilitates the improvement of diagnostic skills by exposing physicians to original cases, connecting images with case histories, and providing a forum for collegial discussion (Thind 2011). Moreover, within the dermatology specialism, TD allows super-specialized referral from second line to a tertiary hospital or center of excellence for diagnostic and/or therapeutic advice (van der Heijden<sup>2</sup> 2010).

Specific TD programs for medical education have also been developed. Initially set up for supervision of dermatology residents (Nelson 2015), the benefits of this type of TD have been extended to medical students (Boyers 2015). This improves the dermatological skills of the FHPs and familiarizes them with TM systems (Lam 2022).

### *2.7. General considerations on teledermatology*

#### *2.7.1. Clinical considerations*

First, TD does not allow to integrate the findings of the palpation of the skin, examination which is sometimes essential for a differential diagnosis. Hence, the assessment of AK with field cancerization or chronic skin disease scoring (e.g. Psoriasis area and severity index (PASI) score in psoriasis) has been demonstrated to be more accurate in FTF visits (Armstrong 2011, Giavina-Bianchi 2020).

Although the implementation of TDS resulted in a significant improvement of skin cancer screening compared to remote clinical imaging, TD does not fit well with a TBE. TDS acquisition of all skin lesions for one patient is much more time-consuming compared to a FTF TBE. Triage of suspicious lesions is necessary, but it cannot completely replace a TBE with the risk of missing a malignant lesion (Aldridge 2013).

Another limitation is that the initial triage is still in hands of the FHPs, that can impact the sensitivity and specificity of skin cancer detection (Tensen 2022).

In general, the safety and survival of a TD system depends on the ability to rapidly refer patients for a FTF control in the case of the detection of a suspicious lesion by the teledermatologist (Abbott 2020).

### *2.7.2. Economic considerations*

Reductions in the number of FTF referrals, workday losses and travel time are all economic arguments supporting TD as a method to reduce costs in population healthcare systems (Pak 2009). However, comprehensive cost assessments of TD are challenging and highly dependent on the established national healthcare system and reimbursement possibilities.

In Europe, the Netherlands were the first to finance a governmental TD system. The 2011 evaluation demonstrated a cost reduction of 18% for TD versus conventional care pathway while maintaining an equivalent quality of healthcare (van der Heijden 2011). As mentioned above, Belgium does not have currently a funded governmental TD system.

At present, financial implications for teledermatologists remain a major limiting factor in the willingness to join a TD program (Armstrong 2011). In fact, TD visits lead to fewer medical procedures and follow-up visits, potentially decreasing earnings (Edison 2012).

### *2.7.3. Societal considerations*

The implementation of a national TD system requires an efficient technical infrastructure and secure telecommunication channels. Furthermore, it is essential to train the users how to work with the program, especially in the correct acquisition of images, which is the one of the most difficult phases to standardize (Norum 2007, Abbott 2020).

In TM market, dermatology experienced the emergence of numerous mobile applications to support SSE (Brewer 2013). Quality assessments demonstrated the low positive and especially negative predictive values of these applications, erroneously comforting the patient (Wolf 2013).

The concept of the digital split must be considered. Younger patients are more likely and prone to use these new technologies. This raises questions about the utility of patient-assisted models for the elderly, where the incidence of skin cancers is considerably higher compared to the younger population (Berndt 2012).

Among the many publications about TM, ethical questions and issues emerged. The main concern is a switch from a patient-focused medicine to a technology-focused medicine. Throughout history, technological advances have always been perceived as a threat of the depersonalization of medicine (Weinberg 2012). This concern may be prevented by an informed consent process about personal data management, benefits, risks, and alternatives to TD (Kluge 2011).

Finally, TM allows dermatologists to work across borders. This opportunity should not lead to some form of exploitation of the patient as a marketing product (Coates<sup>2</sup> 2015).

#### *2.7.4. Legal considerations*

Legal considerations are tributary to the specific legal requirement of each individual country. In Belgium, the General Data Protection Regulation (GDPR) edited by the European Union is used as a reference manuscript for the legal issues around TDS (European Parliament and Council 2016).

Finally, depending on the chosen TD model with up to three parties involved (patient, primary care provider, teledermatologist), the positioning of different medical liabilities must be defined (Coates<sup>2</sup> 2015).

# TELESPOT Project

## 1. Introduction

The development of the application, the study design and the implementation are described in the following publication “Damsin T, Jacquemin P, Canivet G, *et al.* TeleSPOT Project: early detection of melanoma by teledermoscopy in general practice. *Rev Med Liege*, 74(12), 650-654 (2019)” (appendix I).

### 1.1. Ethics

This study was performed in accordance with the Helsinki Convention on Human Rights. The ethics committee and the university hospital legal department approved the project. The patients were informed about all the procedures, and all signed the informed consent forms, and authorized the electronic transfer of clinical data and images (Ethics Committee of the CHU, Sart-Tilman (707), Avenue de l'Hôpital, Liège, B-4000, Belgium).

### 1.2. Study design

PHCs were enrolled in the TELESPOT PhD project. Throughout the study, these centers acquired dermoscopic images of skin lesions judged as suspicious and sent them remotely to the TSCC. After a double reading by two dermatologists, the TSCC sent a triage report, with the primary outcome being the prioritization of lesion management: LPM versus HPM. For HPM lesions, rapid care in the TSCC was proposed.

The study covered two subsequent periods. The initial period (phase 1) included acquisitions from six PHCs, from September 2019 to August 2020. The extension period (phase 2) included data from the six initial PHCs and from three additional PHCs, from September 2020 and August 2022. In fact, a preliminary evaluation was performed after the initial period. This evaluation focused on the raw screening data and its comparison with previous published studies, as well as the satisfaction scores of both involved parties (FHPs and patients). After having achieved the aims of this pilot phase and after the validation of several studied parameters and encouraging feedback from the initial PHCs, it was decided to extend the duration of the study, the number of cases and the number of PHC. A final evaluation was performed after the extension period. This evaluation focused on the statistical analysis of data and its comparison between different groups according to initial versus additional PHCs and initial period versus extension period (table 6). Figure 26 illustrates the study design.

As the high sensitivity and specificity rates of TDS systems were already demonstrated and described above, TELESPOT project did not include a FTF control of all lesions but only for HPM lesions. Previous studies mentioned above showed no significant difference in sensitivity between FTF consultations versus TDS referrals, especially in distinguishing a benign versus malignant lesion. The TELESPOT study design better reflects the final aim of TDS in real-life healthcare conditions: reducing unnecessary FTF visits and accelerating the management of suspicious lesions.

|       | Group 1        | Group 2        | Group 3           | Group 4    |
|-------|----------------|----------------|-------------------|------------|
| PHCs  | 6 initial PHCs | 6 initial PHCs | 3 additional PHCs | All 9 PHCs |
| Phase | Phase 1        | Phase 2        | Phase 2           | Phase 2    |

Table 6 - Groups defined according to initial vs additional PHCs and initial vs extension period



Figure 26 – Study design of TELESPOT project

### 1.3. Description of patient care pathway

Participating PHCs were trained to acquire macroscopic and dermoscopic images for every lesion judged as suspicious with a brief description of patient data. Images were transmitted securely to the TSCC for assessment by two dermatologists. After analysis, a brief report was sent back within five working days to the referring FHP with advice for patient management and diagnosis (figure 27).

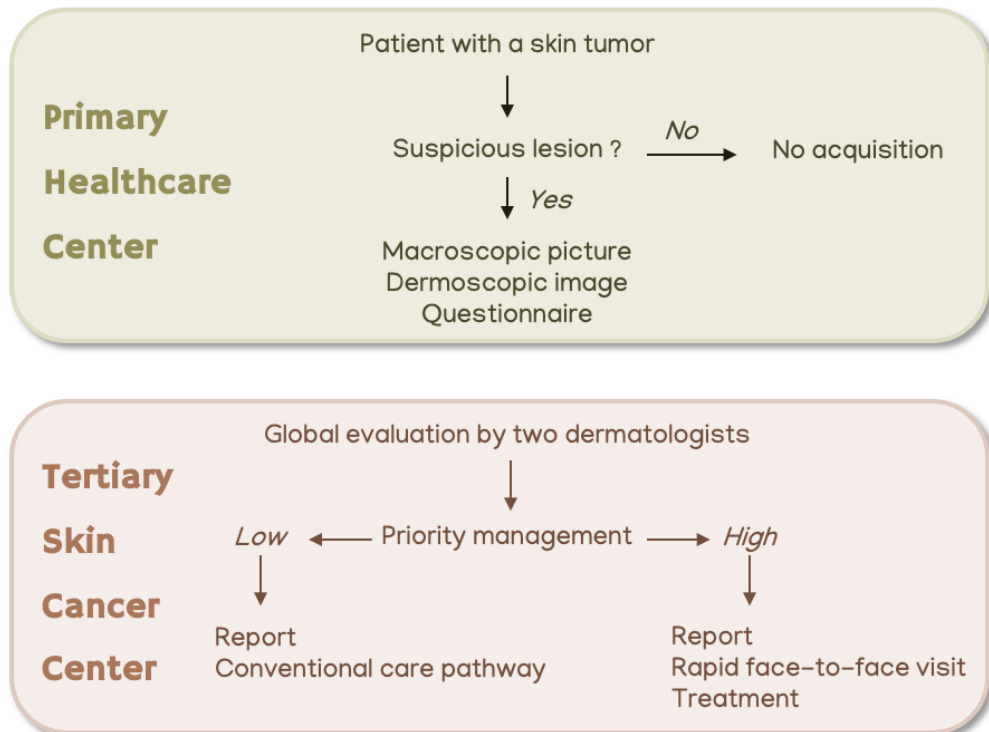


Figure 27 – Detailed TELESPOC pathway

### 1.4. Smartphone application development

To ensure confidentiality and total respect of GDPR, each participant FHP is logged in through a portal authenticator with a unique login and password. The digital identifier can also be used on a smartphone with a mobile number and the Itsme® application, which generates a unique combination guaranteeing secure access to personal data.

Data are uploaded onto the Orthanc® platform, a lightweight open-source digital imaging and communications in medicine (DICOM) server for medical imaging supporting application programming interface representational state transfer (REST) providing interoperability between different computer systems.

The acquired dermoscopic pictures are converted into digital slides. Using whole-slide imaging (WSI), clinical and macroscopic pictures are scanned, and a single high-resolution digital file is created. This is commonly achieved by capturing many small high-resolution image tiles or strips and then converting these into a full image. This conversion accelerates data transfer and visualization of the images. Only the visible files are loaded. The web server is an Apache HTTP server, a free and open-source cross-platform web server software. Patient administrative data are transferred to the hospital information (HIS) system Oasis®. Clinical data are transferred to the electronic patient record (EPR), where they are analyzed, and feedback is generated. Images are also stored into the picture archiving and communication system (PACS) for long-term archiving and internal diffusion with EPR. Data processing is illustrated in figure 28.

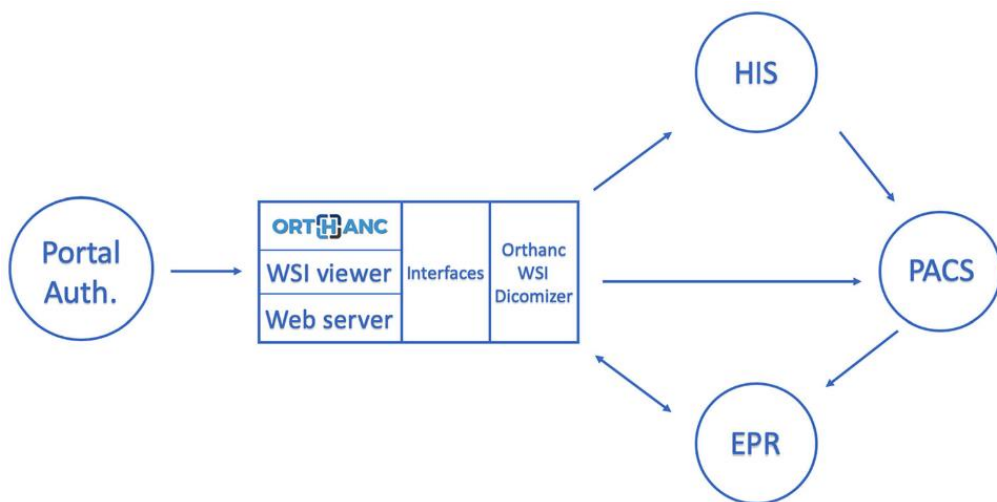


Figure 28 – Data processing in TELESPOt system

### 1.5. Smartphone dermoscopic device

Each PHC is equipped with a smartphone (iPod® Touch 7; Apple, Cupertino, CA, USA) and a handheld dermatoscope compatible with the smartphone (Heine® ic1; Heine Optotechnik, Herrsching, Germany).

### 1.6. Training of primary healthcare centers

Each PHC received a digital presentation (Prezi® software; Prezi® Inc., Budapest, Hungary) with three topics (introduction on pigmented skin lesions, essentials of dermoscopy, and operation of TELESPOt project), a dermoscopy quiz, and an on-site training with the device and application. A second visit was organized after the first cases to improve and/or rectify the quality of acquisitions. Additional on-site visits were at PHC or investigator request.

## 1.7. Demographics

### 1.7.1. *Patient demographics*

The following demographic data were recorded for each patient: age and gender, phototype, indoor versus outdoor profession and a personal and/or familial history of prior skin cancer.

### 1.7.2. *Primary healthcare center demographics*

PHC was considered as close (<20 km) or distant ( $\geq$ 20 km) to the TSCC and as medium size (<10 FHPs in the same PHC) or large ( $\geq$ 10 FHPs). The mean age of FHPs, single versus multiple TELESPOT users in each PHC, and the number of additional teaching visits to the PHCs were recorded.

## 1.8. Outcomes

### 1.8.1. *Primary outcome*

The primary outcome was the number of LPM versus HPM recommendations. For the final evaluation, the primary outcome was compared according to the four groups described above.

### 1.8.2. *Secondary outcomes*

#### 1.1.1.1. *Secondary outcomes about lesions*

Secondary outcomes about lesions included the percentages of malignant lesions among all the recorded lesions, the quality of the acquisition (evaluative versus not-evaluative), the mean time between the TSCC report and the specific care for HPM lesions in comparison with a conventional in-house care pathway, the correlation between the TSCC report for HPM lesions and their histopathological diagnosis, the localization of all the acquired lesions, the duration between the patient's awareness of the lesion and the actual acquisition in the PHC, and the number of acquisitions by PHC per season. In this study, a distinction is made between the malignant or benign nature of a lesion and its management priority. For example, an AK will be categorized as a malignant lesion and assigned a low management priority. The same rationale will apply to an easy-to-treat BCC.



### 1.1.1.2. Secondary outcomes about patient and first-line healthcare provider satisfactions

A modified Likert scale was used to record FHP satisfaction score by telephone visits, assessing ten items (table 7) with a score from 0 (strongly disagree) to 10 (strongly agree). Patient satisfaction was assessed by telephone visits using the same method, with a total of five items and three binary questions (table 8).

| Item   | Score   |
|--|---------|
| The project easily fits into daily practice.                                 | 0 to 10 |
| The acquisition technique is not very time-consuming.                        | 0 to 10 |
| I am satisfied with the triage report and patient care pathway.              | 0 to 10 |
| The project accelerates diagnosis of suspicious skin lesions in my patients. | 0 to 10 |
| The project represents a health benefit for my patient.                      | 0 to 10 |
| I feel more involved in skin cancer screening.                               | 0 to 10 |
| I feel more comfortable diagnosing benign versus malignant skin lesions.     | 0 to 10 |
| I feel more confident about performing a TBE.                                | 0 to 10 |
| The project adds value to PHC.   | 0 to 10 |
| Overall, I am satisfied with the TELESPOT project.                           | 0 to 10 |

Table 7 – FHP satisfaction score

| Item  | Score   |
|---|---------|
| I felt comfortable with the procedure.                | 0 to 10 |
| I felt safe with this new technology.                 | 0 to 10 |
| I trust the specialized advice provided.              | 0 to 10 |
| I would be willing to repeat the TELESPOT experience. | 0 to 10 |
| Overall, I am satisfied with the TELESPOT project.    | 0 to 10 |

| Subsidiary questions  | Answer    |
|---|-----------|
| Did you consult your FHP for this specific lesion or was it your FHP who proposed the analysis? | Yes or no |
| Did you seek a FTF specialist visit to analyze this lesion before TDS project ?                 | Yes or no |
| Did you have an examination of this lesion by a dermatologist after the TDS project?            | Yes or no |

Table 8 – Patient satisfaction score

## 2. Preliminary evaluation: analysis of 1-year initial period

The evaluation of the 1-year initial period has been described in the following publication, or order to determine the clinical feasibility and relevance of the project: “Damsin T, Canivet G, Jacquemin P *et al.* Value of Teledermoscopy in Primary Healthcare Centers: Preliminary Results of the TELESPOT Project in Belgium. *Dermatol Ther (Heidelb)* 10, 1405–1413 (2020). <https://doi.org/10.1007/s13555-020-00445-0>” (appendix II).

### 2.1. Outcomes

#### 2.1.1. Screening data

The following items were assessed: the quality of the acquisition (evaluable versus not-evaluable), the duration between the patient's awareness of the lesion and the actual acquisition in the PHC, the nature of the lesion (benign, malignant or uncertain), the TDS diagnostic category, the management priority (LPM or HPM), the histopathological diagnosis and the correlation with the TSCC report diagnosis, and the mean time between the TSCC report and the specific care for HPM lesions in comparison with a conventional in-house care pathway.

#### 2.1.2. Satisfaction scores

As described above, a modified Likert scale was used to record FHP satisfaction score ( $n = 6$ ) by telephone visits, assessing 10 items with a score from 0 to 10. Patient satisfaction ( $n = 19$ ) was assessed by telephone visits using the same method, with a total of five items and three binary questions.

### 2.2. Statistics

Instead of performing a power calculation, given the limited number of cases, a 95% confidence interval for the proportion of HPM lesions was determined. This confidence interval goes beyond just providing the observed proportion by giving a range of potential values for the proportion studied; it is associated with the observed proportion of HPM lesions, namely 7.6% (8/105; range 1.0–11.8%). Thus, the observed proportion differs from the true one by 5% with a confidence of 95%. Should a lower difference be required, i.e., 3%, at least 300 lesions would have to be included.

## 2.3. Results

### 2.3.1. Screening data

A total of 105 lesions were analyzed from the 77 patients. 67.5% were female. The mean age was 48.5 years (6–89 years).

For 92.4% of lesions, LPM was advised. For the HPM lesions, 75% of TDS diagnosis were confirmed by histology. All NMSC were confirmed. For the melanocytic lesions highly suspected of malignancy, 50% were confirmed as melanoma. Figure 29 compares TDS diagnostic categories versus histopathological diagnosis of HPM lesions.

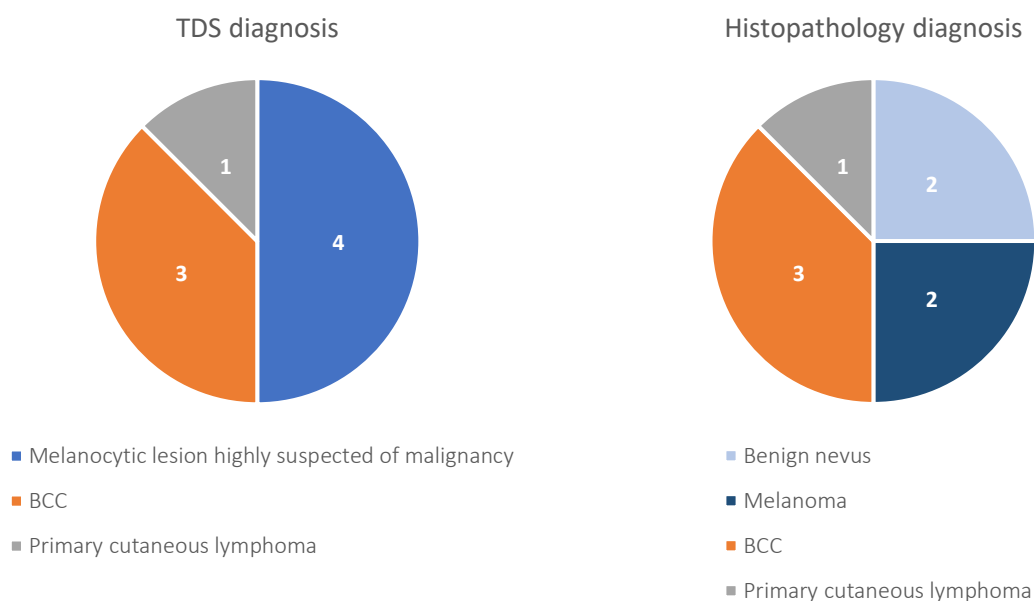


Figure 29 – TDS diagnosis versus histopathology diagnosis for HPM lesions in phase 1

Following TDS assessment, 86.7% of lesions were classified as benign, 5.7% as uncertain, and 7.6% as malignant. Table 9 details the TDS diagnostic categories of all lesions in phase 1. Of the 6 lesions categorized as uncertain, 4 were assigned a high management priority because of their melanocytic origin. Histological analysis confirmed two melanomas (one in situ and one SSM), one Spitz nevus in an adult patient and one congenital nevus. The two lesions assigned a low management priority had a TDS diagnosis of keratoacanthoma versus well-differentiated SCC and a traumatized nevus for which a comparative dermoscopy at 3 months was requested. Overall, 84.8% of TSCC reports were sent with a degree of certainty greater than 8 out of 10.

| Diagnostic category                               | n = 105 (%) |
|---|-------------|
| AK  | 5 (4.8%)    |
| Angioma   | 4 (3.8%)    |
| Atypical nevus                                    | 4 (3.8%)    |
| BCC   | 3 (2.8%)    |
| Benign nevus                                      | 46 (43.8%)  |
| Dermatofibroma                                    | 3 (2.8%)    |
| Keratoacanthoma                                   | 1 (1%)      |
| Lentigo simplex                                   | 7 (6.7%)    |
| Melanocytic lesion highly suspected of malignancy | 4 (3.8%)    |
| Other benign lesions                              | 4 (3.8%)    |
| - Macrocomedo                                     |             |
| - Acanthoma                                       |             |
| - Chondrodermatitis nodularis helioides           |             |
| - Pyogenic granuloma                              |             |
| Seborrheic keratosis                              | 23 (21.9%)  |
| Other malignant lesions                           | 1 (1%)      |
| - Primary cutaneous B lymphoma                    |             |

Table 9 – TDS diagnostic categories in phase 1

A total of three acquisitions were judged as non-evaluable and were asked to be repeated.

According to patients, 49/105 lesions were present for more than one year and 6/105 for less than three months.

The median delay between TDS report and treatment for HPM lesions was 11 days.

### 2.3.2. Satisfaction scores

Using a set of ten questions, physician satisfaction scores were the following:

- 1) the project easily fits into daily practice: 8.6/10
- 2) the acquisition technique is not very time-consuming: 9.4/10
- 3) satisfaction with the report and advice: 9.6/10
- 4) the project accelerates diagnosis of suspicious lesions in my patients: 9/10
- 5) the project represents a health benefit for my patients: 8.8/10
- 6) involvement in skin cancer screening: 8.6/10
- 7) improving competences in benign vs malignant lesions diagnosis: 6.8/10
- 8) more eager to do a complete TBE: 7.6/10
- 9) the project adds value to PHC: 9.2/10
- 10) General satisfaction with the project: 9.4/10

Patient satisfaction results, assessed using five questions, were the following:

- 1) comfort with procedure: 9.4/10
- 2) confidence about this new technology: 8.6/10
- 3) trust in specialized advice: 8.2/10
- 4) willingness to repeat the experience: 8.8/10
- 5) general satisfaction with the project: 8.8/10

Three subsidiary questions were assessed with a binary answer:

- 1) Did you consult your FHP for this specific lesion or was it your FHP who proposed the analysis? 16%: FHP, 84%: patient.
- 2) Did you seek a FTF specialist visit to analyze this lesion before TDS project? 42%: no, 58%: yes.
- 3) Did you have an examination of this lesion by a dermatologist after the TDS project? 16%: yes; 84%: no.

#### 2.4. Discussion

Conclusions of preliminary evaluation will be discussed in the “Global discussion” section.

### 3. Final evaluation: analysis of 3-year period

The 3-year final evaluation of the project is described in the following publication: “Damsin T, Canivet G, Jacquemin P *et al.* Evaluation of a 3-year teledermoscopy project in primary healthcare centres in Belgium. *JEADV Clin Pract.* 2023;1–9. <https://doi.org/10.1002/jvc2.254>” (appendix III).

#### 3.1. Outcomes

Comparisons of endpoints were performed between different groups defined in table 6.

The primary outcome was the number of LPM versus HPM recommendations between the four groups.

Secondary outcomes included the percentages of malignant skin lesions among all the recorded lesions, the quality of the acquisition (evaluable versus not-evaluable), the mean time between the TSCC report and the specific treatment for HPM lesions in comparison with a conventional in-house care pathway, the correlation between the TSCC report for HPM lesions and their histopathological diagnosis, the localization of all the acquired lesions, the duration between the patient's awareness of the lesion and the actual acquisition in the PHC, the number of acquisitions by PHC per season, as well as the patient and FHP satisfaction scores, as previously defined. Wherever relevant, the secondary outcomes were compared between the four groups.

#### 3.2. Statistics

Results are presented as means and standard deviation (SD), quartiles (medians, Q1–Q3) and range (minimum– maximum) for quantitative variables and as frequency tables for qualitative variables. Descriptive statistics as well as comparison between diagnosis and histopathology for HPM lesions are provided on all lesions, in each phase and in each type of PHC in phase 2. The outcomes, that is, nature of the lesion, priority management, repetition, and degree of certainty, were analyzed by a repeated logistic model (genmod) accounting for the fact that some PHCs are included in both phases. In the model, the type of PHC (initial PHCs or additional PHCs) and the study phase were considered as fixed effects and PHC as a random effect. Results are considered significant at the 5% uncertainty level ( $p < 0.05$ ). Analyses were performed using the SAS version 9.4.

### 3.3. Results

#### 3.3.1. Patient demographics

Out of the 335 patients, 56.4% were female (mean age: 50.5 years, min: 2, max: 94 years). The median phototype was 3 (min: 1, max: 6). A minority of patients had an outdoor profession (7.8%). A personal history of prior skin cancer was noted in 3% of the patients. Table 10 illustrates the patient demographics according to the four groups.

| Variable         | Categories | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|------------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|                  |            | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Sex              | Female     | 77                      | 52 (67.5)  | 84                      | 45 (53.6)  | 176                        | 92 (52.3)  | 259                 | 137 (52.9) |
|                  | Male       |                         | 25 (32.5)  |                         | 39 (46.4)  |                            | 84 (47.7)  |                     | 122 (47.1) |
| Phototype        | 1          | 77                      | 3 (3.9)    | 84                      | 3 (3.6)    | 176                        | 2 (1.1)    | 259                 | 5 (1.9)    |
|                  | 2          |                         | 30 (39.0)  |                         | 33 (39.3)  |                            | 63 (35.8)  |                     | 96 (37.1)  |
|                  | 3          |                         | 22 (28.6)  |                         | 24 (28.6)  |                            | 102 (58.0) |                     | 125 (48.3) |
|                  | 4          |                         | 19 (24.7)  |                         | 21 (25.0)  |                            | 8 (4.5)    |                     | 29 (11.2)  |
|                  | 5          |                         | 1 (1.3)    |                         | 2 (2.4)    |                            | 1 (0.6)    |                     | 3 (1.2)    |
|                  | 6          |                         | 2 (2.6)    |                         | 1 (1.2)    |                            | 0 (0.0)    |                     | 1 (0.4)    |
| Profession       | Indoor     | 77                      | 69 (89.6)  | 84                      | 77 (91.7)  | 176                        | 165 (93.8) | 259                 | 241 (93.1) |
|                  | Outdoor    |                         | 8 (10.4)   |                         | 7 (8.3)    |                            | 11 (6.3)   |                     | 18 (6.9)   |
| Personal history | No         | 77                      | 75 (97.4)  | 84                      | 80 (95.2)  | 176                        | 172 (97.7) | 259                 | 251 (96.9) |
|                  | Yes        |                         | 2 (2.6)    |                         | 4 (4.8)    |                            | 4 (2.3)    |                     | 8 (3.1)    |
| Familial history | No         | 77                      | 76 (98.7)  | 84                      | 76 (90.5)  | 176                        | 169 (96.0) | 259                 | 244 (94.2) |
|                  | Yes        |                         | 1 (1.3)    |                         | 8 (9.5)    |                            | 7 (4.0)    |                     | 15 (5.8)   |

Table 10 – Patient demographic data

#### 3.3.2. Primary healthcare center demographics

In phase 1, all the six enrolled PHCs were close to the TSCC and four of the six were considered as large size PHCs. In phase 2, the three additional PHCs were distant to the TSCC, and all were considered as medium size PHCs. Individual data of the PHCs are presented in table 11.

|                               | PHC 1    | PHC 2  | PHC 3    | PHC 4    | PHC 5    | PHC 6  | PHC 7  | PHC 8    | PHC 9    |
|-------------------------------|----------|--------|----------|----------|----------|--------|--------|----------|----------|
| Distance to TSCC (km)         | 15       | 13     | 11       | 11       | 10       | 5      | 115    | 113      | 129      |
| Number of FHP                 | 12       | 4      | 12       | 9        | 13       | 35     | 6      | 7        | 5        |
| Mean age of FHP (years)       | 43.3     | 38.7   | 45.4     | 41.6     | 44.3     | 48.2   | 44.8   | 40.9     | 37.8     |
| User mode                     | Multiple | Single | Multiple | Multiple | Multiple | Single | Single | Multiple | Multiple |
| Additional investigator visit | 3        | 2      | 1        | 1        | 1        | 2      | 1      | 0        | 0        |

Table 11 – PHC demographic data

### 3.3.3. Primary outcome

HPM was recommended in 9.2% of the 478 analyzed lesions, corresponding to 13.1% of the total cohort of 335 patients. Table 12 details the comparison of triage among the four groups. The logistic regression model (genmod) with PHC as random effect and, study phase and type of PHC as fixed effects, shows that the probability of classifying a lesion as HPM is lower for additional PHCs ( $p = 0.023$ ). This probability tends to be higher in phase 2 than in phase 1 but not significant ( $p = 0.057$ ; Table 12).

| Variable            | Categories | All lesions |            | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|---------------------|------------|-------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|                     |            | N           | Number (%) | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Management priority |            | 478         |            | 105                     |            | 115                     |            | 258                        |            | 373                 |            |
|                     | Low        |             | 434 (90.8) |                         | 97 (92.4)  |                         | 97 (84.3)  |                            | 240 (93.0) |                     | 337 (90.3) |
|                     | High       |             | 44 (9.2)   |                         | 8 (7.6)    |                         | 18 (15.7)  |                            | 18 (7.0)   |                     | 36 (9.7)   |

Table 12 – Distribution of HPM versus LPM lesions

### 3.3.4. Secondary outcomes

Of the 478 analyzed lesions, 84.7% were classified as benign, 3.8% as uncertain and 11.5% as malignant. Table 13 details the comparisons between the four groups. The logistic regression model (genmod) with PHC as random effect and, study phase and type of PHC as fixed effects, reveals that the probability of classifying the lesion as malignant is not related to the type of site (initial PHCs or additional PHCs;  $p = 0.64$ ) nor to the phase ( $p = 0.071$ ) but there is a tendency. Indeed, the probability tends to be higher in phase 2 than in phase 1. Table 14 details de TDS diagnostic categories in phase 2.

| Variable             | Categories | All lesions |            | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|----------------------|------------|-------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|                      |            | N           | Number (%) | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Nature of the lesion |            | 478         |            | 105                     |            | 115                     |            | 258                        |            | 373                 |            |
|                      | Benign     |             | 405 (84.7) |                         | 91 (86.7)  |                         | 92 (80.0)  |                            | 222 (86.0) |                     | 314 (84.2) |
|                      | Uncertain  |             | 18 (3.8)   |                         | 6 (5.7)    |                         | 7 (6.1)    |                            | 5 (1.9)    |                     | 12 (3.2)   |
|                      | Malignant  |             | 55 (11.5)  |                         | 8 (7.6)    |                         | 16 (13.9)  |                            | 31 (12.0)  |                     | 47 (12.6)  |

Table 13 – benign, malignant, and uncertain classification



| Diagnostic category                               | n = 373 (%) |
|---|-------------|
| AK  | 16 (4.3%)   |
| Angioma   | 12 (3.2%)   |
| BCC   | 12 (2.8%)   |
| Benign nevus                                      | 152 (40.8%) |
| Dermatofibroma                                    | 10 (2.7%)   |
| SCC   | 12 (3.2%)   |
| Lentigo simplex                                   | 17 (4.6%)   |
| Melanocytic lesion highly suspected of malignancy | 14 (3.8%)   |
| Other benign lesions                              | 18 (4.8%)   |
| - Macrocomedo                                     |             |
| - Wart  |             |
| - Venous lake                                     |             |
| - Molluscum pendulum                              |             |
| - Porokeratosis                                   |             |
| - Condyloma                                       |             |
| Seborrheic keratosis                              | 109 (29.2%) |
| Other malignant lesions                           | 1 (0.3%)    |
| - Dermatofibrosarcoma                             |             |

Table 14 – TDS diagnostic categories in phase 2

In global, 2.1% of the acquisitions were judged as non-evaluable and repetition of image acquisition was required. Table 15 details the comparison in the four groups. The logistic regression model (genmod) with PHC as random effect and, study phase and type of PHC as fixed effects, shows that the probability of a repeated acquisition is not related to the type of site ( $p = 0.14$ ) nor to the phase ( $p = 0.20$ ).

| Variable   | Categories | All lesions |            | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|------------|------------|-------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|            |            | N           | Number (%) | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Repetition | No         | 478         | 468 (97.9) | 105                     | 102 (97.1) | 115                     | 114 (99.1) | 258                        | 252 (97.7) | 373                 | 366 (98.1) |
|            | Yes        |             | 10 (2.1)   |                         | 3 (2.9)    |                         | 1 (0.9)    |                            | 6 (2.3)    |                     | 7 (1.9)    |

Table 15 – Distribution of repetition

For the 44 HPM lesions, the mean interval between the TSCC report and specific treatment was 9 days.

Among the TDS diagnosis of the 44 HPM lesions, 37 (84.1%) were confirmed by histopathology. The TDS diagnoses of NMSC were all confirmed by histopathology. Among the melanocytic lesions highly suspected of malignancy, 11 of the 18 (61.1%) were diagnosed as melanoma (6 in situ melanoma, 4 SSM and 1 LMM). The positive predictive value of the TSCC report for HPM lesions was 83.3% (95% confidence interval: 68.6%–93.0%). Figure 29 compared TDS diagnostic categories versus histopathological diagnosis of HPM lesions in phase 1. Figure 30 compares TDS diagnostic categories versus histopathological diagnosis of HPM lesions in phase 2. Of the 12 lesions categorized as uncertain, 10 were assigned a HPM because of their melanocytic origin. Histological analysis confirmed four melanomas (three in situ and one SSM), one dysplastic nevus, two Spitz nevi in adult patients, one congenital nevus and two traumatized benign nevi. The two lesions assigned a LPM had a TDS diagnosis of irritated seborrheic keratosis and Reed's nevus in a pediatric patient. These two lesions required short-term SDD.

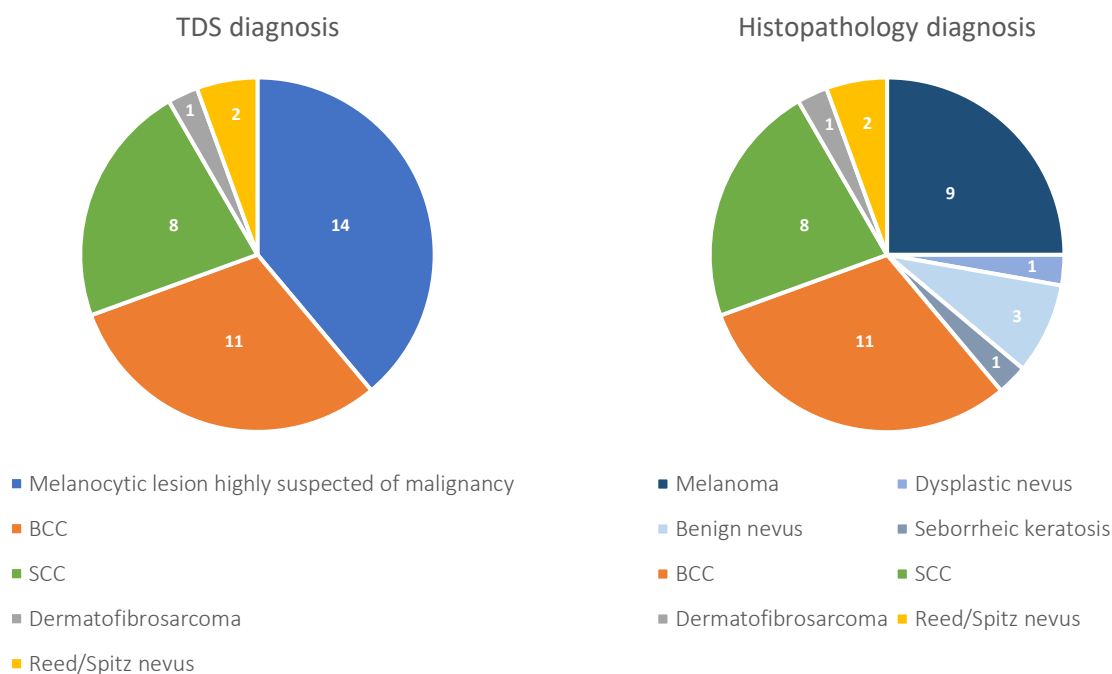


Figure 30 – TDS diagnosis versus histopathology diagnosis for HPM lesions in phase 2

The anatomical distribution of all the lesions was as follows: head and neck (n = 102; 21.3%), trunk (n = 102; 21.3%), upper limbs (n = 81; 16.9%), lower limbs (n = 54; 11.3%) and genital area (n = 4; 0.8%).

The distribution of the interval between the patient's awareness of the lesion and the actual acquisition were: <1 month (n = 53; 11.1%), 1–3 months (n = 73; 15.3%), 3–6 months (n = 46; 9.6%), 6–12 months (n = 75; 15.7%) and >12 months (n = 231; 48.3%). The proportion of HPM lesions among these intervals were 9.4%, 10.3%, 11.6%, 11.7% and 6.5%, respectively.

The seasonal distribution of acquisitions was as follows: spring: 39.5%, summer: 27.6%, autumn: 13% and winter: 19.9%.

Figure 31 highlights the triage of lesions including major data.

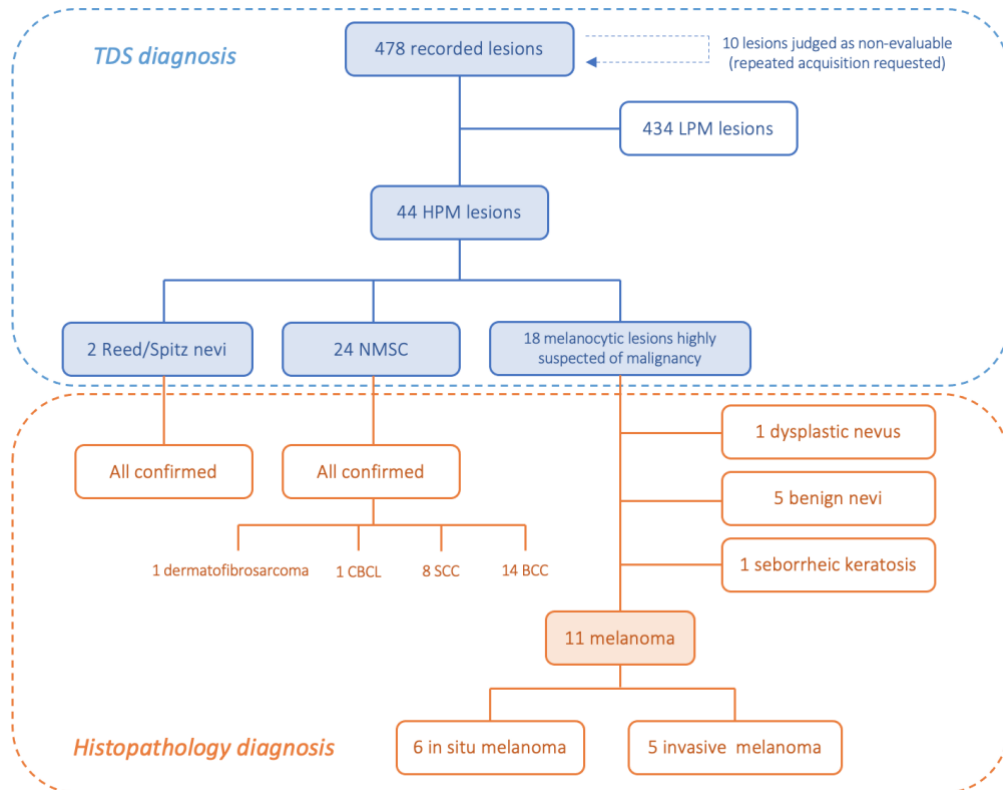


Figure 30 – Triage of recorded lesions with concordance of TDS and histopathology diagnosis

The global satisfaction score of FHPs was 9.4/10 for the initial period and 9.7/10 for the extension period. The global satisfaction score of patients was 8.8/10 and 8.9/10, respectively (table 16).

| FHP satisfaction score   | Phase 1 (n = 6) | Phase 2 (n = 20) |
|--|-----------------|------------------|
| The project easily fits into daily practice.                                 | 8.6/10          | 8.9/10           |
| The acquisition technique is not very time-consuming.                        | 9.4/10          | 9.6/10           |
| I am satisfied with the triage report and patient care pathway.              | 9.6/10          | 9.5/10           |
| The project accelerates diagnosis of suspicious skin lesions in my patients. | 9.0/10          | 9.1/10           |
| The project represents a health benefit for my patient.                      | 8.8/10          | 8.8/10           |
| I feel more involved in skin cancer screening.                               | 8.6/10          | 8.8/10           |
| I feel more comfortable diagnosing benign versus malignant skin lesions.     | 6.8/10          | 7.1/10           |
| I feel more confident about performing a TBE.                                | 7.6/10          | 7.2/10           |
| The project adds value to PHC.   | 9.2/10          | 8.3/10           |
| Overall, I am satisfied with the TELESPOT project.                           | 9.4/10          | 9.7/10           |

| Patient satisfaction score                            | Phase 1 (n = 19) | Phase 2 (n = 64) |
|---|------------------|------------------|
| I felt comfortable with the procedure.                | 9.4/10           | 9.5/10           |
| I felt safe with this new technology.                 | 8.6/10           | 8.7/10           |
| I trust the specialized advice provided.              | 8.2/10           | 8.1/10           |
| I would be willing to repeat the TELESPOT experience. | 8.8/10           | 9.0/10           |
| Overall, I am satisfied with the TELESPOT project.    | 8.8/10           | 8.9/10           |

Table 16 – Detailed FHP and patient satisfaction scores

### 3.4. Discussion

Conclusions of final evaluation will be discussed in the “Global discussion” section.

## 4. Global discussion

### 4.1. Preliminary evaluation

In contrast with the smartphone-based TDS referral system of Börve (iDoc24 PRO®; iDoc24 Inc., Berkeley, CA) (Börve 2015) and the Handyscope® application and FotoFinder Hub® system (FotoFinder Systems GmbH, Bad Birnbach, Germany) used by Vestergaard (Vestergaard<sup>2</sup> 2020), the development of TELESPOT system was based on open-source applications and programs. The main advantages of open-source development are flexibility, sustainability, security, and reduced costs (Reynolds 2011).

The first system (Börve 2015) and TELESPOT application were principally focused on distinguishing benign versus malignant lesions and on prioritizing clinical management. The impact on skin cancer care of TELESPOT TDS referral system was highly appreciated in all PHCs, in good agreement with results from previous reports (Vestergaard<sup>2</sup> 2020, van Sinderen 2019). Patient satisfaction was not assessed in those studies. A limitation in the study design of TELESPOT project was to not include a FTF control visit for LPM lesions. However, the high sensitivity and specificity rates of TDS systems were already demonstrated. These studies showed no significant difference in sensitivity between FTF consultations versus TDS referrals, especially in distinguishing a benign versus a malignant lesion: the diagnostic accuracy for a primary diagnosis and the benign versus malignant triage with TDS were 58.2% (95% CI, 52.3–63.9) and 80.1% (95% CI, 75.0–84.5), respectively (Coates 2015, Vestergaard<sup>1</sup> 2020). In fact, the TELESPOT study design better reflects the final aim of TDS in real-life healthcare conditions: reducing unnecessary FTF visits and accelerating the management of suspicious lesions (Damsin<sup>2</sup> 2022).

Patient demographics were comparable to two other studies: female: 61.4%, mean age: 54 years; female: 63%, mean age: 56 years (Börve 2015, Vestergaard<sup>2</sup> 2020).

Only 2.9% of the acquired images were discarded (low picture quality, out of focus images, or missing macroscopic or dermoscopic images). This value was intermediate regarding the other two studies, reporting 0.4% (Börve 2015) and 9.5% (Vestergaard<sup>2</sup> 2020). This confirms the high reproducibility of dermoscopic image acquisition and underlines the reliability of the system, hence excluding a major bias observed in general TD image acquisition and picture quality.

A total of 86.7% of the lesions were classified as benign and 92.4% as low priority. Melanoma represented 1.9% of all lesions and 25% of HPM lesions. Another study classified 71.9% of lesions as benign versus 28.1% as premalignant/malignant. Melanoma was detected in 4.3%, and LPM was given in 83.8% (Börve 2015). Another study scored 72.3% as benign lesions versus 27.7% as premalignant/malignant lesions, including 3.8% scored as melanocytic malignant lesions (Vestergaard<sup>2</sup> 2020). The last

study did not provide any recommendations in terms of management priority. Of the 6 lesions categorized as uncertain, 4 were assigned a high management priority because of their melanocytic origin. Histological analysis confirmed two melanomas (one in situ and one SSM), one Spitz nevus in an adult patient and one congenital nevus. The two lesions assigned a low management priority had a TDS diagnosis of keratoacanthoma versus well-differentiated SCC and a traumatized nevus for which a comparative dermoscopy at 3 months was requested. Overall, 84.8% of TSCC reports were sent with a degree of certainty greater than 8 out of 10.

For HPM lesions, a FTF visit was scheduled for the week following the triage report, and if necessary, surgery was performed immediately. Management of a HPM lesion was seven times faster in comparison with the conventional in-house care pathway (median waiting time for an FTF visit: 84 days). In Börve's study, this factor was reduced by three (Börve 2015). This difference is possibly explained by the preexisting triage with traditional paper referrals in Sweden in contrast to Belgium, where direct access to specialized care is possible.

A worrying result was that 46.7% of acquired lesions were present for more than 12 months and only 20% were present less than 3 months. No comparable data are available from the other studies (Börve 2015, Vestergaard<sup>2</sup> 2020). This indicates that individuals are still not aware of the risks of skin cancer and that the sooner the diagnosis is made, the better the prognosis is. This stresses once again that repetitions of skin cancer detection programs and awareness campaigns remain mandatory (Nikkels 2004).

The FHP global satisfaction score of 9.4/10 indicated that TELESPOT was easily integrated in PHC. Acquisitions were usually performed by one dedicated FHP. The technique was judged not very time-consuming and considered as a real healthcare benefit for patients. In addition, FHPs felt more active in the fight against skin cancers, although they still tend to refrain from performing a TBE. Lack of time could be an explanation.

In previous studies, the FHP's positive predictive value for malignant/premalignant lesions in general was 49.5%, and 26.3% for melanoma. Indeed, 73.7% of FHPs felt unconfident proposing a diagnosis of melanoma (Vestergaard<sup>2</sup> 2020). Although this study did not directly evaluate this issue, it was indirectly reflected in the 6.8/10 score for the feedback question "improving diagnostic competences in distinguishing benign versus malignant skin lesions." Moreover, a Belgian study evaluated diagnostic ability of FHPs and dermatologists in discriminating pigmented skin lesions: FHPs' versus dermatologists' positive predictive values in discriminating malignant from benign disease were 61% and 92%, respectively. Their respective sensitivity and sensibility percentages were 72% versus 91% and 71% versus 95% (Brochez 2001). Another study revealed that FHP's sensitivity and specificity regarding any malignancy/premalignancy was 87.8% and

59.6%, respectively, and for melanoma, 52.6% and 93.6%, respectively (Vestergaard<sup>2</sup> 2020).

Evaluated after the initial period, the TELESPOT project seems to constitute a helpful tool in PHCs for early skin cancer detection but did not increase willingness to be more involved personally (Damsin<sup>3</sup> 2022). This outsourcing of the intellectual responsibility to a third party was previously observed by other TDS referral systems. Another study found that 97.4% of TDS referrals were reported as helpful by FHPs (van Sinderen 2019).

Finally, patients were highly satisfied with the TELESPOT project based on the global satisfaction score of 8.8/10, although the use of TM is not yet part of their daily life in Belgium (Damsin<sup>4</sup> 2022). These results are in line with other studies reporting patient satisfaction levels of 58.5% (Gilling 2020).

## 4.2. Final evaluation

The pilot phase of the TELESPOT project showed that this TDS system in PHCs represented a useful triage tool for suspicious skin lesions and permitted to adequately prioritize care management (Damsin 2020). The extension phase consolidated the anterior results in a larger cohort and longer evaluation period.

In total, a HPM was recommended in 9.2% of the cases. The proportion of HPM was 7.6% during phase 1 versus 9.7% in phase 2. This could indicate a trend towards an improved triage in the PHCs, but this increase was not statistically significant. However, focusing on the initial PHCs involved in both phases, there was a significant increase in the proportion of HPM lesions (phase 1: 7.6% vs. phase 2: 15.7%, ratio = 2.24). There are two main hypotheses to explain this difference: an external hypothesis and an internal hypothesis. The external hypothesis is based on the fact that the population studied in the extension phase is different from the population in the initial phase. In the extension phase, the female sex ratio tends to decrease (phase 1: 67.5% vs. phase 2: 52.9%), whereas male sex is an accepted independent risk factor for skin cancer (Scoggins 2006). The internal hypothesis is based on the fact that there is a significant improvement in sorting of skin lesions by FHPs over time. Two factors support this last hypothesis. Firstly, a theoretical concept known as the cognitive intuitive learning process, a way of acquiring knowledge or skills that relies heavily on intuition and the subconscious mind (Gachon 2005). Secondly, comparing the proportion of HPM lesions in the extension phase between the initial and additional PHCs, there is also a significant difference in favor of the initial PHCs (HPM lesions from initial PHCs in phase 2: 15.7% vs. HPM lesions from additional PHCs in phase 2: 7.0%,  $p = 0.023$ ).

The classification of lesions according to their nature in phase 2 was: 84.2% benign, 12.6% malignant and 3.2% uncertain. Of the 12 lesions categorized as uncertain, 10 were assigned a HPM because of their melanocytic origin. Histological analysis confirmed four melanomas (three in situ and one SSM), one dysplastic nevus, two Spitz nevi in adult patients, one congenital nevus and two traumatized benign nevi. The two lesions assigned a LPM had a TDS diagnosis of irritated seborrheic keratosis and Reed's nevus in a pediatric patient. These two lesions required short-term SDD.

The clinical and/or dermoscopic images were judged as non-evaluable in 2.1% of the cases and a second acquisition of the lesion was required. This value ranged between two other similar studies, reporting 0.4% (Börve 2015) and 9.5% (Vestergaard<sup>2</sup> 2020) as non-evaluable. There was no significant difference in percentages between the three additional PHCs compared to the six initial PHCs. This demonstrates that PHCs are immediately competent in acquiring dermoscopic images.



The mean interval between an HPM triage report and a FTF visit (and surgery if needed) was 9 days, nine times faster in comparison with the conventional care pathway (median waiting time for a dermatology visit in Belgium: 81 days). This highly significant acceleration of management underlines the efficiency of the TDS system in the fight against skin cancer.

Out of all the lesions recommended for HPM, 84.1% were histopathologically confirmed. All lesions classified as NMSC were histopathologically confirmed. Among the melanocytic lesions highly suspected of malignancy, 61.1% were histopathologically confirmed as melanoma with more than half (54.5%) as in situ stage. This fact could be explained by the sole participation in the project, increasing awareness, and maybe also by speeding up the delay between the diagnostic suspicion and the factual surgery. However, larger series and longer observations will be required to validate or not this fact. Melanoma represented 2.3% of all analyzed lesions and 25% of all the HPM lesions. These data were comparable to other studies (Börve 2015). The seven melanocytic lesions clinically and dermoscopically highly suspected of malignancy classified for which histopathology excluded melanoma comprised: two Spitz nevi, one dysplastic naevus, two congenital nevi, one benign naevus and one seborrheic keratosis. Globally, the positive predictive value of the TSCC report for HPM lesions was 83.3% (95% confidence interval: 68.6%–93.0%).

In both periods, it was remarkable to observe that 48.3% of the lesions sent in for advice were present for more than 12 months. Only 26.4% were present less than 3 months. This indicates that one out of two individuals are still not aware of the risks of skin cancer and that the sooner the diagnosis is made, the better the prognosis is. In contrast, the message about the link between sun exposure and skin cancer seems better known. Indeed, more than two out of three lesions were acquired during the spring and summer months (Nikkels 2004, Garbe<sup>2</sup> 2022).

The FHP and patient satisfaction scores were excellent and maintained stable between phases 1 and 2. These results are well in line with other studies reporting FHP and/or patient satisfaction levels (Vestergaard 2021, van Sinderen 2022, Gilling 2020). The TDS system confirms its general usefulness, easy implementation, and user-friendliness.

The main limitation of a TDS system remains the initial triage in PHCs. Rare clinical presentations such as amelanotic melanoma are still easily missed (Detrixhe 2016). A recent retrospective study compared the initial self-reported referral decisions of FHPs before TDS system versus their final self-reported referral decisions after TDS system for skin lesions diagnosed by TD as (pre)malignant or benign. In half of the TDS consultations, FHPs adjusted their initial referral decision after TD advice and TD diagnosis. Initially, FHPs did not have the intention to refer 56.8% of patients with a malignant TDS diagnosis and 16.0% of patients with a premalignant TD diagnosis but then decided to refer these patients after the TDS consultation. Moreover, FHPs adjusted their decision from referral to non-referral in 74.9% of

benign skin lesions (Tensen 2022). Furthermore, the study design of TELESPOOT project did not include a FTF control visit for LPM lesions. However, the high sensitivity and specificity rates of TDS systems were already demonstrated. These studies showed no significant difference in sensitivity between FTF consultations versus TDS referrals, especially in distinguishing a benign versus a malignant lesion: the diagnostic accuracy for a primary diagnosis and the benign versus malignant triage with TDS were 58.2% (95% CI, 52.3–63.9) and 80.1% (95% CI, 75.0–84.5), respectively (Coates 2015, Vestergaard<sup>1</sup> 2020). In fact, the TELESPOOT study design better reflects the final aim of TDS in real-life healthcare conditions: reducing unnecessary FTF visits and accelerating the management of suspicious lesions (Damsin<sup>2</sup> 2022). Another limitation could be that a TDS system is not fitted for TBE (Viola 2011). If the acquisition of a lesion takes less than 2 minutes, every single lesion on the patient would have to be acquired independently, which would be too time-consuming for the PHC. Finally, the TELESPOOT project is still considered an opportunistic secondary prevention tool. Firstly, in terms of the selection of PHCs, as the current roll-out of the project has not made it possible to recruit all the PHCs in Belgium. Finally, within a PHC itself, the decision to acquire a lesion was made on an individual scale, and the project did not represent a mass screening tool for the entire PHC patient base. However, this last point may be balanced by the fact that the project is being promoted within the participating PHCs, thereby raising awareness among a part of the patient population that was, until now, perhaps still unaware of the risks associated with skin cancers.

In conclusion, this long-term evaluation indicates the added value of this TDS for PHCs, delivering a high FHP and patient satisfaction, an efficient tool for an accelerated management of a suspicious lesion and an effective triage as well as avoiding unnecessary patient travel and specialized care visits. In addition, this evaluation showed that long-term participation resulted in a 2.24-fold improved triage quality of the PHCs.

## 5. Summary

The incidence of melanoma and non-melanoma skin cancer (NMSC) is steadily rising over years and leads to an increased workload for first-line healthcare providers (FHP) and dermatologists. Furthermore, the increasing scarcity of dermatologists and long waiting times hamper rapid diagnosis and management, with a potential risk for worse prognoses.

Triage in primary healthcare centers (PHC) could be useful, but FHPs often lack faith in their clinical diagnoses. Teledermoscopy (TDS), defined as dermoscopic images that are analyzed at distance using telecommunication technologies, may help to distinguish skin lesions and speed up the management of suspicious lesions. Finally, in terms of public health, early diagnosis followed by appropriate management remains the cornerstone of reduced skin cancer morbidity and mortality.

In 2019, a pilot TDS project named “TELESPOT” (TELEdermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce) was initiated (Damsin 2019). PHCs were enrolled in the TELESPOT PhD project. Throughout the study, these centers acquired dermoscopic images of skin lesions judged as suspicious and sent them remotely to a tertiary skin cancer center (TSCC). After a double reading by two dermatologists, the TSCC sent a triage report, with the primary outcome being the prioritization of lesion management: low-priority management (LPM) versus high-priority management (HPM). For HPM lesions, rapid care in the TSCC was proposed.

The study covered two subsequent periods. The initial period (phase 1) included acquisitions from six PHCs, from September 2019 to August 2020. The extension period (phase 2) included data from the six initial PHCs and from three additional PHCs, from September 2020 and August 2022.

A preliminary evaluation was performed after the initial period (Damsin 2020). This evaluation focused on the raw screening data and its comparison with previous published studies, as well as the satisfaction scores of both involved parties (FHPs and patients). A total 86.7% of lesions were classified as benign and 92.4% as LPM. Melanoma represented 1.9% of all lesions and 25% of HPM lesions. For HPM lesions, a face-to-face (FTF) visit was scheduled for the week following the sorting report and if necessary, surgery was performed immediately. Specific treatment of a HPM lesion was seven times faster in comparison with the conventional care pathway (median waiting time for a FTF visit: 84 days). These data were in line with those of previous studies. Global satisfaction scores of FHPs and patients were respectively 9.4/10 and 8.8/10. A limitation in the study design of TELESPOT project was to not include a FTF control visit for LPM lesions. However, the high sensitivity and specificity rates of TDS systems were already demonstrated. These studies showed no significant difference in sensitivity between FTF consultations versus TDS referrals, especially in triage of benign versus malignant lesion. The preliminary report on the TELESPOT project showed its general usefulness, easy implementation, and user-friendliness. Both FHPs

and patients judged the TELEPSOT system as highly beneficial for improved quality of healthcare. Speed of management of suspicious lesions was increased seven-fold by reducing unnecessary FTF visits. In fact, these encouraging results from the preliminary evaluation led to the extension of the study.

A final evaluation was performed after the extension period (Damsin 2023). This evaluation focused on the statistical analysis of data and its comparison between different groups according to initial versus additional PHCs and initial versus extension period. Finally, a second evaluation of satisfaction scores was conducted. In total, an HPM was recommended in 9.2% of the cases. The proportion of HPM was 7.6% during phase 1 versus 9.7% in phase 2. This could indicate a trend towards an improved triage in the PHCs, but this increase was not statistically significant. However, when evaluating the 6 PHCs who participated in both periods, there was a statistically significant improvement in triage (phase 2: 15.7% vs. phase 1: 7.6%: ratio = 2.24). Hence, the PHCs became more performant over time in discriminating the skin lesions. The clinical and/or dermoscopic images were judged as non-evaluable in 2.1% of the cases and a second acquisition of the lesion was required. There was no significant difference in percentages between additional PHCs compared to initial PHCs. This demonstrates that PHCs are immediately competent in acquiring dermoscopic images. The mean interval between an HPM triage report and a FTF visit (and surgery if needed) was 9 days, nine times faster in comparison with the conventional care pathway (median waiting time for a dermatology visit in Belgium: 81 days). This highly significant acceleration of management underlines the efficiency of the TDS system in the fight against skin cancer. Out of all the lesions recommended for HPM, 84.1% were histopathologically confirmed. All lesions classified as NMSC were histopathologically confirmed. Among the melanocytic lesions highly suspected of malignancy, 61.1% were histopathologically confirmed as melanoma with more than half (54.5%) as in situ melanoma. Globally, the positive predictive value of the TSCC report for HPM lesions was 83.3% (95% confidence interval: 68.6%–93.0%). In both periods, it was challenging to observe that 48.3% of the lesions sent in for advice were present for more than 12 months and only 26.4% were present less than 3 months, according to the patient. This indicates that one out of two individuals are still not aware of the risks of skin cancer and that the sooner the diagnosis is made, the better the prognosis is. The FHP and patient satisfaction scores were excellent and maintained stable between phases 1 and 2. The main limitation of a TDS system remains the initial triage in PHCs. Rare clinical presentations such as amelanotic melanoma are still easily missed.

In conclusion, this long-term evaluation indicates the added value of this TDS for PHCs, delivering a high FHP and patient satisfaction, an efficient tool for an accelerated management of a suspicious lesion and an effective triage as well as avoiding unnecessary patient travel and specialized care visits. In addition, this evaluation showed that long-term participation resulted in a 2.24- fold improved triage quality of the PHCs.

*L'incidence des cancers de la peau est en nette et constante augmentation depuis maintenant plusieurs années. Cette situation entraîne une surcharge de travail pour les professionnels de santé de première ligne et les dermatologues. En outre, la relative pénurie de dermatologues et les délais d'attente pour un rendez-vous chez le médecin spécialiste de plus en plus longs sont des facteurs limitant un diagnostic ainsi qu'une prise en charge médicale rapide, pouvant théoriquement conduire à une aggravation du pronostic.*

*La réalisation d'un tri en Médecine de première ligne pourrait être une solution à explorer. Cependant, les ressources théoriques et logistiques de cette Médecine de première ligne sont le plus souvent manquantes. La télédermoscopie, définie comme l'analyse à distance d'images dermoscopiques grâce aux technologies de télécommunication, peut être un outil dans le tri de ces lésions cutanées et ainsi accélérer la prise en charge des lésions suspectes. En effet, en termes de santé publique, un diagnostic précoce suivi d'une prise en charge appropriée reste la pierre angulaire de la diminution de la morbidité et de la mortalité liées au cancer cutanés.*

*En 2019, un projet pilote de télédermoscopie appelé "TELESPOT" (TELEdermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce) a été lancé (Damsin 2019). Des centres de Médecine de première ligne ont été recrutés afin de participer à ce projet. Tout au long de l'étude, ces centres ont eu l'opportunité de réaliser des clichés dermoscopiques de lésions cutanées jugées suspectes et de les envoyer à un hôpital universitaire pour une analyse à distance. Après une double lecture par deux dermatologues, un rapport de tri était établi, avec comme résultat principal la priorisation de la prise en charge de la lésion ; soit une prise en charge de priorité faible ou bien une prise en charge de priorité élevée. Pour les lésions nécessitant une prise en charge de priorité élevée, un trajet de soin rapide était proposé dans le centre universitaire ayant établi le rapport de tri.*

*L'étude a couvert deux périodes. La phase initiale dont les acquisitions de six centres de Médecine de première ligne ont été réalisées entre septembre 2019 et août 2020, et la phase d'extension dont les acquisitions des six centres de Médecine de première ligne ainsi que de trois centres supplémentaires ont été réalisées entre septembre 2020 et août 2022.*

*Une évaluation préliminaire a été réalisée après la phase initiale (Damsin 2020). Cette évaluation s'est concentrée sur les données brutes de l'étude et leur comparaison avec des précédentes publications sur un système de télédermoscopie. La satisfaction des centres ainsi que des patients vis-à-vis du projet a également été étudiée. Au total, 86,7% des lésions ont été classées comme bénignes et 92,4% ont été catégorisées comme lésions avec une priorité de prise en charge faible. Les mélanomes représentaient 1,9% de toutes les lésions et 25% des lésions avec une priorité de prise en charge élevée. Pour les lésions avec une priorité de prise en charge élevée, un contrôle en vie réelle était programmée dans la semaine suivant le rapport de tri et si nécessaire, une sanction chirurgicale était réalisée dans le même temps.*

*Comparativement au parcours de soins conventionnel avec un délai moyen de prise en charge médicale estimé à 84 jours, les lésions avec une priorité de prise en charge élevée ont vu leur parcours de soins accéléré d'un facteur sept. Ces données sont comparables à celles d'études antérieures. Les scores de satisfaction globale des centres et des patients étaient respectivement de 9,4/10 et de 8,8/10. L'une des principales limites du plan d'étude du projet TELESPOOT fut de ne pas inclure de visite de contrôle en vie réelle des lésions avec une priorité de prise en charge faible. Cependant, la performance de la télédermoscopie a déjà été démontrée par le passé. Les études n'ont pas montré de différence significative de sensibilité entre les consultations en vie réelle et les avis de télédermoscopie, en particulier pour le tri des lésions bénignes par rapport aux lésions malignes. Ainsi, l'évaluation préliminaire du projet TELESPOOT a démontré son utilité générale, sa facilité de mise en œuvre et sa convivialité. Tant les centres de Médecine de première ligne que les patients ont jugé le projet comme une valeur ajoutée dans la qualité des soins de santé. Le délai de prise en charge de lésions jugées suspectes a été réduit par sept. Parallèlement, de nombreuses visites en Médecine tertiaire jugées inutiles ont pu être évitées. C'est en réalité ces résultats encourageants obtenus lors de cette évaluation préliminaire qui ont mené à une extension de l'étude.*

*L'évaluation finale a été réalisée après la période d'extension (Damsin 2023). Cette évaluation s'est concentrée sur l'analyse statistique des données et leur comparaison entre les différents groupes, selon qu'il s'agissait de centres de Médecine de première ligne recrutés dès la phase initiale ou ceux recrutés pour la phase d'extension, ainsi que de la période d'acquisition. Une seconde évaluation des scores de satisfaction a également été réalisée. Au total, une priorité de prise en charge élevée a été recommandée dans 9,2% des cas. Tout centre confondu, la proportion de lésions avec une priorité de prise en charge haute était de 7,6 % au cours de la phase initiale contre 9,7% au cours de la phase d'extension. Si une tendance se dessine quant à l'amélioration du tri dans les centres de Médecine de première ligne entre les deux phases, cette différence n'était pas statistiquement significative. Toutefois, l'évaluation des six centres ayant participé aux deux phases de l'étude a mis en évidence une amélioration statistiquement significative du tri (phase 2 : 15,7% de lésions avec une priorité de prise en charge élevée en phase d'extension contre 7,6% en phase initiale, ratio = 2,24). Cette donnée démontre l'amélioration des performances de tri de la Médecine de première ligne au fil du temps. Les images cliniques et/ou dermoscopiques ont été jugées non-évaluables dans 2.1% des cas et une seconde acquisition de la lésion a été nécessaire. Aucune différence significative n'a été retrouvée entre la qualité d'acquisition des centres initiaux et des centres additionnels, démontrant le caractère immédiat et effectif de l'acquisition d'images dermoscopiques par les centres de Médecine de première ligne. Pour une lésion avec une priorité de prise en charge élevée, le délai moyen du trajet de soins a été réduit d'un facteur neuf, toujours en comparaison avec le parcours de soins conventionnel. Cette accélération significative de la prise en charge souligne l'efficacité de la télédermoscopie dans la lutte contre les cancers cutanés. Sur l'ensemble des lésions avec une priorité de prise en charge élevée, 84,1% des diagnostics dermoscopiques*

*ont été confirmés à l'histologie. Toutes les lésions catégorisées comme des cancers cutanées hors mélanome ont été confirmées à l'histologie. Parmi les lésions mélanocytaires hautement suspectes de malignité, 61,1% ont été confirmées histologiquement comme des mélanomes, dont plus de la moitié (54,5%) à un stade in situ. Globalement, la valeur prédictive positive du rapport de tri émanant du centre universitaire pour les lésions avec une priorité de prise en charge élevée était de 83,3% (intervalle de confiance à 95% : 68,6%-93,0%). Dans les deux phases, 48,3% des lésions envoyées pour avis étaient présentes depuis plus de 12 mois et seules 26,4% étaient présentes depuis moins de 3 mois, selon le patient. Indirectement, cette donnée met en exergue qu'une personne sur deux n'est toujours pas consciente des risques du cancer de la peau et que plus le diagnostic est précoce, meilleur est le pronostic. Les scores de satisfaction de la période d'extension étaient excellents et maintenus par rapport à la phase initiale. La principale limite d'un système de télédermoscopie en Médecine de première ligne reste le tri initial. En effet, certaines présentations cliniques plus rares de mélanome, comme les mélanomes achromiques, peuvent encore facilement passer inaperçues.*

*En conclusion, cette évaluation à long terme démontre la valeur ajoutée de ce système de télédermoscopie en Médecine de première ligne, tout en offrant une grande satisfaction des centres et des patients. Le système représente un outil profitable pour une prise en charge accélérée d'une lésion suspecte par le biais d'un tri efficace, tout en évitant une proportion importante de visite en vie réelle en centre universitaire jugée inutile. Enfin, cette évaluation a montré que la participation à long terme a permis de multiplier par 2,24 la qualité du tri dans les centres de Médecine de première ligne.*

## 6. Perspectives

### 6.1. Sustainability of the TELESPOt project

Although the TELESPOt system was designed to be as realistic as possible in medical daily practice, it remains a doctoral project that will have to be confronted with real-life integration in the not-too-distant future. This integration will depend on several factors.

First, as the developer of the TELESPOt project, the sustainability of the system can be considered from two main directions. The first option is framing the TDS project in a governmental setting. Although this option is not currently available in Belgium, the competent authorities are making progress on the matter (Heselmans 2022). On the authorities' side, the TELESPOt project has solid data on possible savings in terms of healthcare costs through a significant reduction in unnecessary referrals to specialized medicine. Furthermore, although the healthcare systems are not directly comparable, the Netherlands has demonstrated financial savings of 18% with the integration of TD (van der Heijden 2011). On the developer side, there are several arguments in favor of integrating the TELESPOt project into a government framework. Firstly, governmental projects often benefit from stable funding sources, reducing financial uncertainties. Again, from a financial point of view, both the honoraria of the referring doctor and the teledermatologist and the reimbursement of the patient comply with the conventional rules of healthcare insurance. Secondly, access to resources, whether material or human, is facilitated. In fact, integrating a teledermoscopy system on a national scale requires dedicated infrastructures and involves many players (Abbott 2020). And thirdly, a TDS system associated with a government institution can enhance the public's trust in the project, especially in healthcare-related technologies. Alongside the benefits of an integrated government approach, there are a couple of limitations. First, governmental processes can be slow and bureaucratic, potentially affecting the project's agility. Moreover, stricter regulatory compliance and oversight may be required, which could increase the project's complexity. Finally, as the team that initiated the project, its integration into a government framework could lead to a certain loss of control over decision-making. Alternatively, a startup to drive the sustainability of the TELESPOt project could be considered. This option also offers a different set of advantages and challenges. In general, startups are known for their agility, enabling faster innovation and adaptation to needs of the field. This characteristic was very quickly apparent in the PhD project, which can be compared to a not-for-profit startup. In addition, the autonomy of the project is preserved, with more control over its direction, technology, and decision-making. However, a startup process implies a financial risk and a requirement to comply with market regulations, as well as healthcare standards. In the context of Belgium's specific circumstances, it might be worth exploring the availability of government support or incubators for healthcare startups. In fact, a hybrid model, allowing involvement of public healthcare institutions while maintaining some autonomy, could ultimately be considered as the optimal solution.



While the TELESPOT project has demonstrated effective collaboration between FHPs and tertiary medicine, the secondary level of healthcare has not been considered. In a healthcare system that remunerates healthcare professionals on a fee-for-service basis, the positioning of private dermatologists can be a challenge. TBE represents a significant proportion of consultations in private practice, while mass screening has not proven its effectiveness. For example, in the United States, TBE and the analysis of a cutaneous tumor lesion represent the top two reasons for visiting a dermatologist, accounting for at least 20% of all consultations (Peck 2022). Thus, the implementation of a TDS system could potentially reduce the profits generated by private dermatologists, also due to the absence of technical procedures possible in TD. In the specific situation of the TELESPOT project, envelope funding could be an attractive option. Based on the projected savings, part of this funding would be dedicated to providing the equipment for the PHCs, while another part would be used to pay the teledermatologist a fixed fee. Although there is currently a legal fee code for teleconsultation, a necessary condition is that there must already be a therapeutic relationship with the patient, which is not the case with the TDS system.

## 6.2. Dedicated dermoscopy training for first-line healthcare providers

Although the final evaluation of the TELESPOT project highlighted an improvement in the performance of the triage carried out in the PHCs over time, the project was initially a tool for outsourcing the dermoscopic analysis of a suspicious skin lesion. In addition, this project demonstrated a certain degree of disempowerment of taking a diagnostic decision on the behalf of the PHCs. However, still with the idea of involving first-line medicine in the early detection of skin cancers, another approach to explore would be to train FHPs specifically in dermoscopy.

Numerous studies have focused on the formation of FHPs for the early detection of skin cancers, with or without the use of dermoscopy. A review published in 2022 concluded that integrating dermoscopy into the training of FHPs increased the performance of this first-line screening (Gonna 2022). The main limitation remains the imperative necessity of initial training in the use of dermoscopy. In fact, using dermoscopy without training is deleterious in terms of diagnostic performance. Without specific training, it is preferable for FHPs to rely on “naked eye” clinical examination (Kittler 2002).

Another Belgian PhD project has focused specifically on dermoscopy training for PHCs. At first, a new dermoscopic algorithm based on the TADA algorithm was developed. Specially designed for FHPs, it enabled global learning of the dermoscopic characteristics of the most common skin tumors while minimizing the time and complexity involved (Harkemanne<sup>1</sup> 2023). Finally, a comparative study was performed of a long versus short dermoscopy learning program in first-line medicine. The non-inferiority of the short learning program was demonstrated, on condition that regular refresher sessions were carried out (Harkemanne<sup>2</sup> 2023).

While at first sight the outsourcing of dermoscopic analysis and the dedicated training of FHPs in dermoscopy appear to be at odds, a hybrid model could in fact represent the optimal approach. Thanks to their specific training, FHPs would be able to carry out the most effective initial triage possible, while at the same time having the opportunity to refer lesions with a dermoscopic image highly suspicious of malignancy or difficult to interpret to a TSCC remotely. This last step remains crucial for ensuring the connection between first-line and specialist medicine, and thus for rapid patient management.

### 6.3. Artificial intelligence

In a research project where the cornerstone is the integration of new technologies in the field of healthcare, the topic of AI is unavoidable. However, it is essential to remember that the TELESPOT project does not rely on AI but on new telecommunications technologies, with the dermoscopic analysis of lesions still being performed by the human.

AI is defined as the ability of a machine to display human-like capabilities such as reasoning, learning, planning, and creativity. AI enables technical systems to perceive their environment, deal with what they perceive, solve problems and act to achieve a specific goal. There are many areas of application for AI, and healthcare is one of them (European parliament 2023).

In the field of onco-dermatology, the analysis of dermoscopic images by AI is a hot topic. Indeed, there are an increasing number of studies comparing the diagnostic performance of humans versus AI. Recently, a multicenter and prospective clinical trial compared humans and AI performance in diagnosing and managing pigmented skin lesions. These two main groups were subsequently subdivided into two subgroups: specialists and novices for the human group, and two different computer algorithms for the AI group. Regarding the diagnostic performance, one of the two AI algorithms demonstrated non-inferiority compared with specialists and was significantly superior compared with novices. Regarding the management performance, the same AI algorithm failed to demonstrate its non-inferiority over both novices and specialists. In addition, this study highlighted that the choice of AI algorithm itself influences performances (Menzies 2023).

Beyond the sensationalism that these studies pitting humans against computers can sometimes provoke, the emergence of a new technology such as AI in the field of healthcare comes with its own set of benefits, but also its own set of challenges, as do the new telecommunication technologies. In brief, the advantages of AI for skin cancers diagnosis are the following: early detection, AI systems can analyze a large number of skin lesions quickly and accurately; consistency, AI systems maintain concordance in assessments, limiting the risk of human error due to factors such as fatigue or subjectivity; scalability, AI systems can be exploited at scale to serve a larger patient cohort; access to specialized medicine, AI systems can assist FHPs in areas with limited access to dermatologists and thus improve healthcare equity; Data Integration, AI algorithms can integrate and analyze various data sources to provide a more comprehensive diagnosis. In contrast, the limitations of AI for skin cancers diagnosis are the following: data quality, AI models rely largely on the quality and quantity of data for training and biased or incomplete data can lead to inaccurate results; misdiagnosis, no algorithm has been able to demonstrate infallible performance and the risk of false positives or false negatives is definitely present; lack of interpretability, it is sometimes difficult to correlate the AI decision-making process with a clinical outcome due to the complexity of computer algorithms; ethical and

privacy concerns, large-scale use of sensitive patient data raises legal and ethical issues; overreliance on AI, healthcare providers may develop a uncritical confidence in this AI and potentially reducing their own expertise and clinical judgment (Sangers 2023).

In summary, while AI offers an unprecedented potential in improving the early skin cancer detection, careful consideration of its advantages and risks is crucial in its implementation in clinical practice. Effective collaboration between the various players is essential to get the best out of AI and limit its drawbacks.

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# Addendum

## 1. Publications in research area

### 1.1. Main publications as first author

1.1.1. Damsin T, Jacquemin P, Canivet G, et al. TeleSPOT Project : early detection of melanoma by teledermoscopy in general practice. Rev Med Liege, 74(12), 650-654 (2019) (Appendix I)

## LE PROJET TELESPOT : Détection précoce du mélanome par Télédermoscopie en Médecine Générale

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DAM SIN TH (1), JACQUEMIN P (2), CANIVET G (3), GIET D (4), GILLET P (5), NIKKELS AF (6)

**Résumé :** Depuis des décennies, l'incidence des cancers cutanés est en nette augmentation. Cette tendance alarmante s'applique également au mélanome. Il représente le 4<sup>ème</sup> cancer le plus fréquent chez la femme en 2015. Une prise en charge précoce permet de réduire la morbidité et la mortalité. Le dépistage représente la pierre angulaire de la prévention secondaire. Néanmoins, l'accès au diagnostic fiable et rapide est entravé par plusieurs facteurs limitants, notamment l'accessibilité à une Médecine spécialisée. Une des solutions à cette problématique est de collaborer avec la Médecine de première ligne par le biais de la télédermatologie. Le projet TeleSPOT, acronyme de Teledermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce, a pour objectif de fournir une aide diagnostique à distance par des dermatologues afin de trier les lésions cutanées pigmentées suspectes et d'en accélérer la prise en charge.

**MOTS-CLÉS :** Mélanome - Dépistage - Médecine générale - Télédermatologie - Dermoscopie

**TELESPOT PROJECT : EARLY DETECTION OF MELANOMA BY TELEDERMOSCOPY IN GENERAL PRACTICE**

**SUMMARY :** Since decades the incidence of skin cancer is clearly rising. This alarming trend also applies to melanoma. It represents the 4th most common cancer in women and 6th in men in 2015. Early recognition and treatment reduce both morbidity and mortality. Screening is the cornerstone of secondary prevention. However, access to reliable and rapid diagnosis is hampered by several factors, including accessibility to specialized medicine. One of the solutions to this problem is to collaborate with the first-line medical care through a teledermatology system. The TeleSPOT project, Teledermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce, aims to provide a remote diagnostic aid by dermatologists to distinguish suspect pigmented skin lesions and accelerate their management.

**KEYWORDS :** Melanoma - Screening - General practice - Teledermatology - Dermoscopy

### INTRODUCTION

L'incidence des cancers cutanés (carcinomes basocellulaires (BCC) et spinocellulaires cutanés (cSCC), mélanome, carcinome de Merkel) est en nette et constante augmentation depuis des décennies. En Belgique, celle-ci est passée de 11.000 nouveaux cas en 2004 à 37.000 nouveaux cas en 2015 (1, 2). Si la majorité des tumeurs malignes cutanées est représentée par le BCC dont le potentiel métastatique est extrêmement faible, cette tendance alarmante s'applique également au mélanome. En 2016, 3.069 nouveaux cas ont été recensés, ce qui correspond à une augmentation annuelle d'environ 5 % depuis 2004 (1, 2). Par ailleurs, cette augmentation est spéculée à 49 % pour 2025 (2). Le mélanome représente le 4<sup>ème</sup> cancer le plus fréquent chez la femme et le 6<sup>ème</sup> chez l'homme en 2015 (nouveaux diagnostics de cancer, cancers de la peau non-mélanomes [BCC et cSCC] exclus, enregistrés en Belgique) (1, 2).

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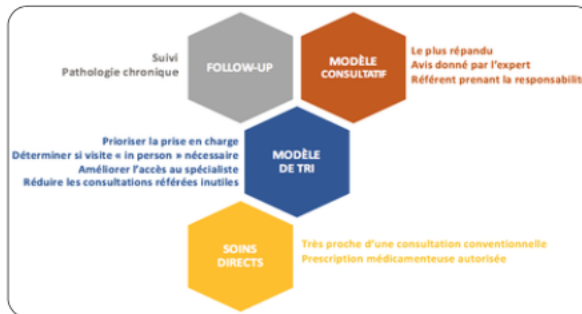
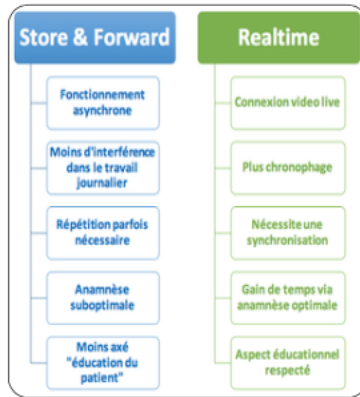
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## TÉLÉDERMATOLOGIE

La télédermatologie se définit comme l'application de la télémédecine au domaine de la dermatologie. Développée depuis les années 90, elle permet de prodiguer une aide diagnostique et thérapeutique pour la médecine de première ligne se trouvant éloignée des centres secondaires et tertiaires. Elle comporte différentes modalités de fonctionnement (Figure 1) et différents types de pratique, à savoir : suivi, consultatif, tri et soins directs (Figure 2) (6).

**Figure 1. Avantages et inconvénients des 2 modalités de fonctionnement de la télédermatologie.**



**Figure 2. Types de pratique de la télédermatologie.**

Par rapport à la télédermatologie où on utilise des photographies et/ou des films des lésions, la télédermoscopie a l'avantage d'une prise d'image standardisée qui est peu sujette aux variations dans la qualité de l'acquisition d'images (5, 20, 21). En effet, après humidification de la lésion à l'aide de l'alcool à 70 %, le verre de contact est directement posé sur la lésion à étudier et à photographier.

## LE PROJET TELESPOT

Le projet TeleSPOT, développé dans le cadre du nouveau Centre Intégré d'Oncologie du CHU de Liège, aura pour but de fournir une aide diagnostique face à une lésion cutanée pigmentée et d'en accélérer la prise en charge si nécessaire.

L'analyse des images cliniques et dermoscopiques envoyées par les centres de médecine générale participant au centre tertiaire d'analyse (Figure 3) sera effectuée dans le service de Dermatologie du CHU de Liège par deux dermatologues.

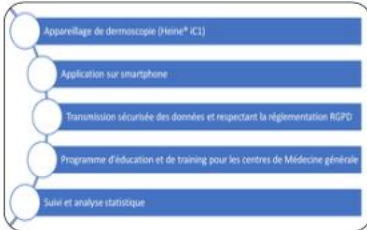
Ce projet utilisera donc la modalité «store and forward» (Figure 1), avec un modèle de tri et intégrera un système de dermoscopie. Sa mise en place nécessite une certaine infrastructure technique, informatique et logistique (Figure 4).

Les centres de soins primaires recrutés désigneront un médecin -ou un infirmier- qui recevra une formation de base en dermoscopie, afin de pouvoir faire un premier tri entre les lésions pigmentées mélanocytaires (naevi, mélanomes, etc.) et les lésions non pigmentées non mélanocytaires (kératoses séborrhéiques pigmentées, carcinomes basocellulaires pigmentés, etc.).

**Figure 3.** Trajet de l'information dans le projet TeleSPOT entre la médecine de première ligne et le centre de soins tertiaire.



**Figure 4.** Matériaux et méthodes du projet TeleSPOT.



Pour les lésions jugées suspectes, une anamnèse dermatologique succincte (Figure 5), ainsi que l'acquisition d'une image macroscopique et dermoscopique seront effectuées dans des conditions standardisées. Les images macroscopiques et dermoscopiques ainsi que les données du patient seront encodées sur une application spécialement développée à cette fin, respectant le RGPD (Règlement Général sur la Protection des Données). Ces données seront, ensuite, transmises de façon sécurisée au service de Dermatologie qui réalisera une double lecture et émettra un rapport de tri. Ce dernier sera transmis au médecin traitant, endéans les 5 jours ouvrables (Figure 6).

Soit la lésion est jugée bénigne et ne nécessite donc aucune suite, soit la lésion est hautement suspecte de malignité et un conseil de prise en charge rapide sera délivré. Pour les lésions intermédiaires ou difficiles à classer, une visite auprès d'un dermatologue sera conseillée. La Figure 7 résume le projet TeleSPOT.

**Figure 5.** Anamnèse dermatologique succincte sur l'application sur smartphone.

|                                   |   |
|-----------------------------------|---|
| Phototype                         |   |
| Métier                            | <ul style="list-style-type: none"> <li>• Intérieur</li> <li>• Extérieur</li> </ul>  |
| Antécédent personnel de mélanome  | <ul style="list-style-type: none"> <li>• Non</li> <li>• Oui (+ localisation et année)</li> </ul>  |
| Antécédent familial de mélanome   | <ul style="list-style-type: none"> <li>• Non</li> <li>• Oui (+ membre de la famille)</li> </ul>   |
| Localisation de la lésion         | <ul style="list-style-type: none"> <li>• Menu déroulant</li> <li>• Champ libre</li> </ul>   |
| Délai de progression de la lésion | <ul style="list-style-type: none"> <li>• Moins d'1 mois</li> <li>• Entre 1 et 3 mois</li> <li>• Entre 3 et 6 mois</li> <li>• Entre 6 et 12 mois</li> <li>• Plus de 12 mois</li> </ul> |

**Figure 6.** Rapport de tri généré après double lecture et renvoyé au médecin demandeur.

|                            |  |
|----------------------------|--|
| Nature de la lésion        | <ul style="list-style-type: none"> <li>• Bénigne</li> <li>• Maligne</li> <li>• Incertaine</li> </ul>                     |
| Proposition diagnostique   | • Champ libre  |
| Coefficient de certitude   | • Echelle de 1 à 10  |
| Priorité de trajet de soin | <ul style="list-style-type: none"> <li>• Faible (dans les 12 semaines)</li> <li>• Haute (dans les 2 semaines)</li> </ul> |

## DISCUSSION

La dermoscopie est un outil facile à utiliser, développé dans un premier temps comme aide diagnostique des lésions pigmentaires. Cependant, progressivement, son utilisation s'est élargie vers de nombreuses pathologies inflammatoires, oncologiques et infectieuses de la peau. La dermoscopie est progressivement entrée dans les outils diagnostiques indispensables en Dermatologie et, actuellement, la

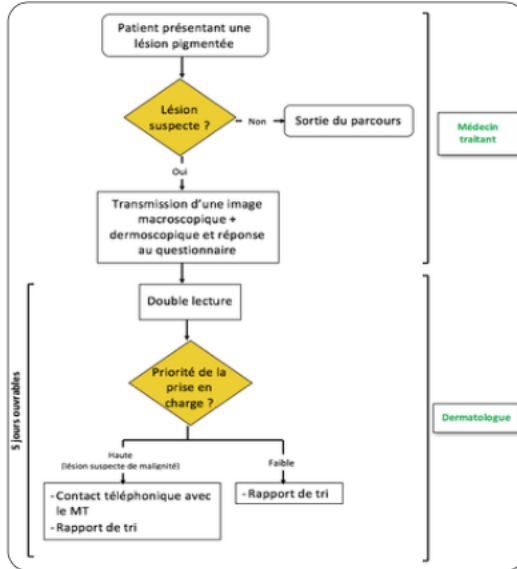


Figure 7. Résumé schématique du projet TeleSPOT.

jeune génération est systématiquement formée à cette technique. Il est démontré que la sensibilité et la spécificité des diagnostics s'améliorent avec l'expérience du dermatologue. L'analyse des images dermoscopiques peut se faire selon différents algorithmes, plus ou moins complexes, plus ou moins faciles à apprendre et à utiliser en pratique quotidienne. Citons le système ABCD (asymétrie, étude des bords, couleur, structures dermoscopiques et score dermoscopique total, > 5,4 jugé comme hautement suspect), l'algorithme Australien de Menzies (critères positifs et négatifs), la liste Italienne en 7 points, l'analyse des patrons architecturaux, CASH (22). Cependant, en pratique clinique, le travail du dermatologue se base sur un processus de reconnaissance globale de type cognitif, prenant en compte divers éléments issus d'images mémorisées de lecture et de l'expérience.

Dans un futur proche, l'analyse des lésions suspectes se fera vraisemblablement aider par l'intelligence artificielle. En effet, en 2016, l'International Skin Imaging Collaboration Melanoma Project a réalisé une étude comparant la précision diagnostique de dermatologues expérimentés *versus* des algorithmes informatiques dans

le diagnostic de mélanome à partir d'images dermoscopiques (23-27). Les algorithmes informatiques individuels ont montré des performances similaires à celles des dermatologues expérimentés. Cependant, les techniques de fusion, c'est-à-dire combinant différents algorithmes, permettent une amélioration significative des performances informatiques, avec une spécificité dépassant celle de l'humain (23-27).

## CONCLUSION

Les systèmes de télédermatologie sont une aide précieuse dans le diagnostic et la prise en charge à distance des problèmes dermatologiques. La fiabilité et l'utilité clinique sont bien établies. La télédermoscopie est un nouvel outil fournissant un système de tri ainsi qu'une aide diagnostique devant des lésions pigmentées suspectes. La phase de test étant terminée avec succès, le projet TeleSPOT sera mis à la disposition de certains centres de Médecine de première ligne participants. Son utilité pour la pratique quotidienne sera évaluée à 1 et à 2 ans.



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BRIEF REPORT

## Value of Teledermoscopy in Primary Healthcare Centers: Preliminary Results of the TELESPOT Project in Belgium

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### ABSTRACT

**Introduction:** Teledermoscopy using smartphone-based applications is becoming more and more important in a setting of increasing frequency of skin cancer and difficult access to specialized care. The TELESPOT project aimed to provide rapid diagnosis and speed up patient

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flow between primary healthcare centers and a tertiary care center in Belgium. The aim of the present study is to describe the development of an in-house smartphone-based dermoscopy application, evaluate its real-life value in a series of primary healthcare centers, and present preliminary diagnostic data.

**Methods:** Modified Likert scales were used to assess patient and general practitioner (GP) satisfaction rates for the system. Furthermore, a total of 105 photographic and dermoscopic images were acquired in a series of 80 patients at participating centers.

**Results:** Overall, patient and GP satisfaction levels were 89% and 94%, respectively. High-priority management was recommended in 7.6% of cases (8/105: 3 basal cell carcinoma, 1 primary cutaneous B-cell lymphoma, 1 Spitz melanocytic nevus, 1 congenital nevus, 1 in situ melanoma, and 1 invasive melanoma, proven by histology).

**Conclusions:** The primary healthcare centers were highly satisfied with the TELESPOT project in terms of user-friendliness, efficacy, and reliability as well as in providing a reinforced image of first-line medicine efforts in combating skin cancer.

**Keywords:** Melanoma; Primary healthcare; Public health; Skin cancer; Teledermatology; Teledermoscopy

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**Key Summary Points**

The TELESPOt project is based on a teledermoscopy device and smartphone application to be used for skin cancer detection in primary healthcare centers.

Both physicians and patients participating in the TELESPOt teledermoscopy project reported very high satisfaction levels.

In terms of skin cancer management in primary healthcare centers, teledermoscopy is a useful tool to preselect patients and allows rapid access to specialized care.

**DIGITAL FEATURES**

This article is published with digital features to facilitate its understanding. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.12906749>.

**INTRODUCTION**

The incidence of skin cancer, including basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (cSCC), melanoma, and Merkel cell carcinoma, has been steadily increasing for decades [1, 2]. This evolution has led to a higher workload for general practitioners (GPs) and dermatologists. Preselection of patients could avoid unnecessary specialist visits. In addition, insufficient awareness from the general population and care providers at primary healthcare centers (PHCs), distance to specialized diagnostic centers, and long waiting lists for appointments are other factors that hamper early diagnosis [3, 4]. In terms of public health, early diagnosis remains the cornerstone of reducing skin cancer morbidity and mortality [5].

Although dermoscopy has steadily increased the diagnostic accuracy of skin cancer, its use is

limited in first-line medicine [6, 7]. Teledermoscopy (TDS) allows image analysis at a distance. This is less operator dependent compared with teledermatology, as acquisition of images is standardized and highly reproducible [8]. The sensitivity and specificity of TDS have been established previously [9].

This background initiated the TELEDermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce (TELESPOt) project [8]. Participating PHCs were trained to acquire macroscopic and dermoscopic images for every lesion judged as suspect with a brief description of patient data. Images were transmitted securely to a tertiary center for analysis by two experienced dermatologists. After analysis, a brief report was sent back within 5 working days to the GP with advice for patient management and diagnosis if possible (Fig. 1).

This article describes the TELESPOt project and aims to assess patient and GP satisfaction levels. Furthermore, preliminary data on management advice and diagnostic results are presented.

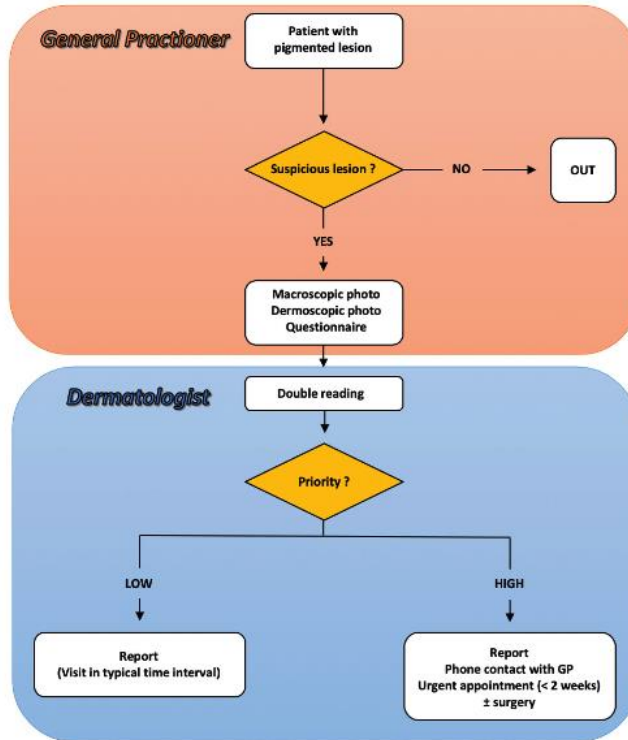
**METHODS**

This study was performed in accordance with the Helsinki convention on human rights. The ethics committee of CHU du Sart-Tilman and the university hospital legal department approved the project. Patients were informed about all procedures, and they all signed informed consent forms.

**Smartphone Application Development**

Each participant GP is logged in through a portal authenticator with a unique login and password. The digital identifier can also be used on a smartphone with a mobile number and the Itsme® application, which generates a unique combination guaranteeing secure access to personal data.

Data are uploaded onto the Orthanc® platform, a lightweight open-source digital imaging and communications in medicine (DICOM) server for medical imaging supporting application programming interface representational



**Fig. 1** Workflow in TELESPOT project

state transfer ( REST) providing interoperability between different computer systems.

The acquired dermoscopic pictures are converted into digital slides. Using whole-slide imaging (WSI), clinical and macroscopic pictures are scanned, and a single high-resolution digital file is created. This is commonly achieved by capturing many small high-resolution image tiles or strips and then converting these into a full image. This conversion accelerates data transfer and visualization of the images. Only the visible files are loaded. The

web server is an Apache HTTP server, a free and open-source cross-platform web server software. Patient administrative data are transferred to the hospital information system Oazis®. Clinical data are transferred to the electronic patient record (EPR), where they are analyzed and feedback is generated. Images are also stored into the picture archiving and communication system (PACS) for long-term archiving and internal diffusion with EPR. Data processing is shown in Fig. 2.

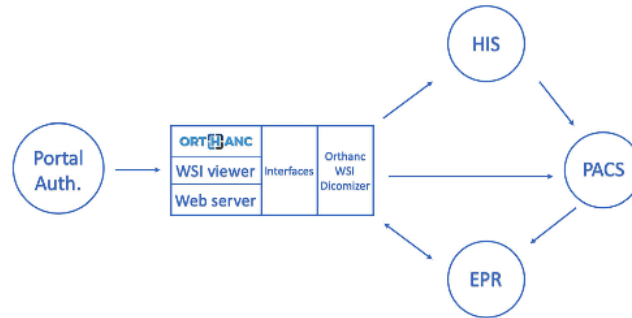


Fig. 2 Data processing in TELESPOt system

#### Smartphone Dermoscopic Device

Each PHC is equipped with a smartphone (iPod® Touch 7; Apple, Cupertino, CA) and a handheld dermatoscope compatible with the smartphone (Heine® ic1; Heine Optotechnik, Herrsching, Germany).

#### Training of PHC and Visits

Each PHC received a digital presentation (Prezi® software; Prezi® Inc., Budapest, Hungary) with three topics—introduction on pigmented skin lesions, essentials of dermoscopy, and operation of TELESPOt project—a dermoscopy quiz, and an on-site training with the device and application. A second visit was organized after the first cases to improve and/or rectify the quality of acquisitions. Other on-site visits were at PHC or investigator request.

#### Project Settings

Six PHCs were selected within a 15-km radius of the tertiary center. All PHCs work with a multidisciplinary team, totaling 42 GPs (mean age: 44 years), 22 nurses, and other paramedical/administrative staff.

#### Screening Items

The following items were assessed: quality of acquisition, evolution of lesion over time, nature of lesion, diagnosis, management priority with specific management recommendations according to the proposed TELESPOt diagnosis (Table 1), histopathology of high-priority lesions, time to face-to-face (FTF) visit, and/or surgery for high-priority lesions.

#### Satisfaction Scores

A modified Likert scale was used to record physician satisfaction score ( $n = 6$ ) by telephone visits, assessing 10 items with a score from 0 to 10. Patient satisfaction ( $n = 19$ ) was assessed by telephone visits using the same method, with a total of five items and three binary questions.

#### Statistics

Instead of performing a power calculation, given the limited number of cases, a 95% confidence interval for the proportion of high-priority lesions was determined. This confidence interval goes beyond just providing the observed proportion by giving a range of potential values for the proportion studied; it is associated with the observed proportion of high-priority lesions, namely 7.6% (8/105;

**Table 1** Distribution of diagnoses on TELESPOt acquired images

| Diagnostic category  | n = 105 (%) | Specific management     |  |
|--|-------------|-------------------------|--|
|  |             | Priority recommendation | Treatment recommendation                 |
| Actinic keratosis  | 5 (4.8%)    | Low                     | Cryotherapy or other destructive therapy |
| Angioma  | 4 (3.8%)    | Low                     | Abstention                               |
| Atypical nevus   | 4 (3.8%)    | Low                     | Closed follow-up                         |
| Basal cell carcinoma   | 3 (2.8%)    | High                    | Surgery                                  |
| Benign nevus   | 46 (43.8%)  | Low                     | Follow-up                                |
| Dermatofibroma   | 3 (2.8%)    | Low                     | Abstention                               |
| Keratoacanthoma  | 1 (1%)      | Low                     | Abstention                               |
| Lentigo simplex  | 7 (6.7%)    | Low                     | Follow-up                                |
| Melanocytic lesion highly suspected of malignancy  | 4 (3.8%)    | High                    | Surgery                                  |
| Other benign lesions (macrocomedo, acanthoma, chondrodermatitis nodularis helioides, and pyogenic granuloma) | 4 (3.8%)    | Low                     | According to diagnosis                   |
| Seborrheic keratosis   | 23 (21.9%)  | Low                     | Abstention                               |
| Other malignant lesions (primary cutaneous B lymphoma)   | 1 (1%)      | High                    | Surgery                                  |

range 1.0–11.8%). Thus, the observed proportion differs from the true one by 5% with a confidence of 95%. Should a lower difference be required, i.e., 3%, at least 300 lesions would have to be included.

## RESULTS

### Satisfaction Scores

Using a set of 10 questions, physician satisfaction scores were the following: (1) the project easily fits into daily practice: 8.6/10; (2) the acquisition technique is not very time-consuming: 9.4; (3) satisfaction with the report and advice: 9.6; (4) the project accelerates diagnosis of suspicious skin lesions in my patients: 9; (5) the project represents a health benefit for my patients: 8.8; (6) involvement in skin cancer screening: 8.6; (7) improving diagnostic

competences in distinguishing benign versus malignant skin lesions: 6.8; (8) more eager to do a complete skin check-up: 7.6; (9) the project adds value to PHC: 9.2; and (10) general satisfaction with the project: 9.4.

Patient satisfaction results, assessed using five questions, were the following: (1) comfort with procedure: 9.4; (2) confidence about this new technology: 8.6; (3) trust in specialized advice: 8.2; (4) willingness to repeat the experience: 8.8; and (5) general satisfaction with the project: 8.8. Three subsidiary questions were assessed with a binary answer: (1) did you consult your GP for this specific lesion or was it your GP who proposed the analysis? 16%: GP, 84%: patient; (2) did you seek an in-person appointment with a dermatologist to analyze this lesion? 42%: no, 58%: yes; and (3) did you have an examination of this lesion by a dermatologist after the TDS project? 16%: yes; 84%: no.

### Screening Results

A total of 105 lesions were analyzed. Among the 80 patients, 67.5% were female. The mean age was 48.5 years (6–89 years). A total of three acquisitions were judged as impossible to assess and were asked to be repeated. According to patients, 49/105 lesions were present > 1 year and 6/105 < 3 months. Following double-blinded assessment of clinical data and clinical and dermoscopic images, 86.7% of lesions were classified as benign, 5.7% as uncertain, and 7.6% as malignant (Table 1). Specific management was issued for every single case. For 92.4% of lesions, low-priority management was advised. High-priority advice was given for three basal cell carcinoma, one primary cutaneous B-cell lymphoma, one Spitz melanocytic nevus, one congenital nevus, one in situ melanoma, and one invasive melanoma. All clinical diagnoses were histopathologically confirmed. The median delay between TELEPSOT diagnosis and treatment for high-priority lesions was 11 days.

### DISCUSSION

In contrast with the smartphone-based TDS referral system of Börve (iDoc24 PRO<sup>®</sup>; iDoc24 Inc., Berkeley, CA) [10] and the Handyscope<sup>®</sup> application and FotoFinder Hub<sup>®</sup> system (FotoFinder Systems GmbH, Bad Birnbach, Germany) used by Vestergaard [11], the development of our system was based on open-source applications and programs. The main advantages of open-source development are flexibility, sustainability, security, and reduced costs [12].

The first system [10] and our application are principally focused on distinguishing benign versus malignant lesions and on prioritizing clinical management. The impact on skin cancer care of our TDS referral system was highly appreciated in all PHCs, in good agreement with results from previous reports [11, 13]. Patient satisfaction was not assessed in those studies.

As very high sensitivity and specificity rates of the TDS system have already been published, our study did not include an FTF control. In

fact, no significant difference in sensitivity was observed between FTF consultations and TDS referrals, especially concerning distinguishing benign versus malignant: diagnostic accuracy for primary diagnosis and benign versus malignant triage with TDS were 58.2% (95% CI 52.3–63.9) and 80.1% (95% CI 75.0–84.5), respectively [9]. In detail, this situation reflects better the final aims of TDS in real-life health-care conditions: downsizing unnecessary FTF visits and accelerating management of suspicious lesions.

Our demographics are comparable to two other studies: female: 61.4%, mean age: 54 years; female: 63%, mean age: 56 years [10, 11].

Only 2.9% of the acquired images were discarded (low picture quality, out of focus images, or missing macroscopic or dermoscopic images). This value is intermediate regarding the other two studies, reporting 0.4% [10] and 9.5% [11]. This confirms the high reproducibility of image acquisition and underlines the reliability of the system, hence excluding an important bias observed in general teledermatology image acquisition and picture quality.

A total 86.7% of lesions were classified as benign and 92.4% as low priority. Melanoma represented 1.9% of all lesions and 25% of high-priority lesions. Another study classified 71.9% of lesions as benign versus 28.1% as premalignant/malignant. Melanoma was detected in 4.3%, and low priority was given in 83.8% [10]. Another study scored 72.3% as benign lesions versus 27.7% as premalignant/malignant lesions, including 3.8% scored as melanocytic malignant lesions [11]. The last study did not provide advice in terms of management priority.

For high-priority lesions, an FTF visit was scheduled for the week following the sorting report, and if necessary, surgery was performed immediately. Management of a high-priority lesion was seven times faster in comparison with the conventional care pathway (median waiting time for an FTF visit: 84 days). In Börve's study, this factor was reduced by three [10]. This difference is possibly explained by the preexisting triage with traditional paper

referrals in Sweden in contrast to Belgium, where direct access to specialized care is possible.

A worrying result was that 46.7% of acquired lesions were present for more than 12 months and only 20% were present less than 3 months. No comparable data are available from the other studies [10, 11]. This indicates that individuals are still not aware of the risks of skin cancer and that the sooner the diagnosis is made, the better the prognosis is. This stresses once again that repetitions of skin cancer detection programs and awareness campaigns still remain mandatory [14].

In contrast with the initial aim of providing a diagnostic aid for pigmented lesions, a large number of lesions turned out to be nonpigmented, suggesting a need for diagnostic help at PHCs not only for pigmented lesions.

The high global satisfaction score of 9.4/10 indicates that TELESPOt was easily integrated at PHCs. Acquisitions were usually performed by one dedicated GP or nurse. The technique was judged not very time-consuming and considered as a real healthcare benefit for patients. In addition, GPs felt more active in the fight against skin cancers, although they still tend to refrain from performing a total body examination. Lack of time could be an explanation.

The GP's positive predictive value for malignant/premalignant lesions in general was 49.5%, and 26.3% for melanoma [11]. Indeed, 73.7% of GPs felt unconfident proposing a diagnosis of melanoma [11]. Although this study did not directly evaluate this issue, it was indirectly reflected in the 6.8/10 score for the feedback question "improving diagnostic competences in distinguishing benign versus malignant skin lesions." Moreover, a Belgian study evaluated diagnostic ability of GPs and dermatologists in discriminating pigmented skin lesions: GPs' versus dermatologists positive predictive values in discriminating malignant from benign disease were 61% and 92%, respectively [15]. Their respective sensitivity and sensibility percentages were 72% versus 91% and 71% versus 95% [15]. Another study revealed that GPs' sensitivity and specificity in regards to any malignancy/premalignancy was

87.8% and 59.6%, respectively, and for melanoma, 52.6% and 93.6%, respectively [11].

Evaluated at 6 months, the TELESPOt project seems to constitute a helpful tool at PHCs for early skin cancer detection, but did not increase willingness to be more involved personally. This outsourcing of a task to a third party was previously observed by other TDS referral systems. Another study found that 97.4% of TDS referrals were reported as helpful by GPs [13].

This type of project could be helpful as diagnostic aid in many settings, such as improving dermatological care in developing countries [4].

Finally, patients were highly satisfied with the TELESPOt project (global satisfaction: 8.8/10), although use of telemedicine and telermatology is not yet part of their daily life in Belgium. Our results are in line with other studies reporting patient satisfaction levels of 58.5% [16].

One limitation to our system (and to other TDS systems) remains the initial triage deciding whether a lesion is to be analyzed or not, which may miss rare clinical presentations such as amelanotic melanoma [7]. However, the classification of more than 90% of acquisitions as low-priority management indirectly indicates the possibility of an effective screening at PHCs. In addition, the fact that only 7/105 lesions were sent with a prediagnosis is another indicator that outsourcing of this diagnostic act is preferred.

## CONCLUSIONS

This preliminary report on the TELESPOt project confirmed its general usefulness, easy implementation, and user-friendliness. Both PHCs and patients judged the TELESPOt system as highly beneficial for improved quality of healthcare. Speed of management of suspicious lesions was increased sevenfold by reducing unnecessary FTF visits. Long-term evaluation will determine its final place in the fight against skin cancer.



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**Authorship.** All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Disclosures.** Thomas Damsin, Gregory Canivet, Pauline Jacquemin, Laurence Seidel, Pierre Gillet and Didier Giet have nothing to disclose. Arjen F. Nikkels is a member of the journal's Editorial Board.

**Compliance with Ethics Guidelines.** This study was performed in accordance with the Helsinki convention on human rights. The ethics committee of CHU du Sart-Tilman and the university hospital legal department approved the project. The patients were informed about all the procedures and all signed the informed consent forms.

**Data Availability.** All data generated or analysed during this study are included in this published article/as supplementary information files.

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ORIGINAL ARTICLE



## Evaluation of a 3-year teledermoscopy project in primary healthcare centres in Belgium

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None

**Abstract**

**Background:** With the increasing incidence of skin cancer and limited access to specialised care, teledermoscopy (TDS) may represent a useful triage tool for skin cancer detection.

**Objectives:** An evaluation of a 3-year TDS project in primary healthcare centres (PHCs) in Belgium (TELESPOT project).

**Methods:** A total of nine PHCs were trained to use an in-house developed smartphone-based application for macroscopic and dermoscopic acquisition of skin lesions, subsequently analysed independently by two investigators in a tertiary university skin cancer centre. The primary outcome was the proportion of high-priority management (HPM) recommendations. Secondary outcomes included the TDS diagnoses, the quality of image acquisition, the mean time between HPM recommendations and subsequent surgery, the correlation between HPM reports and histopathology after surgery as well as patient and general practitioner satisfaction scores. All the endpoints were compared between the initial year of the TDS project and the subsequent 2-year extension period of the study.

**Results:** Over 3 years, a total of 478 lesions were analysed in 335 patients: initial phase (105 lesions from 76 patients in six PHCs) and extension phase (373 lesions from 259 patients in nine PHCs). An HPM was recommended in 9.2% (initial and extension phases: 7.6% and 15.7%, respectively). The dermoscopic-histological correlation achieved 84.1%. The median delay between HPM and surgery was 9 days.

**Conclusions:** This TDS project avoided unnecessary tertiary care visits in about 9 out of 10 cases, increased the HPM by a ninefold in comparison with the conventional care pathway and provided excellent satisfaction levels for PHCs and patients. Long-term participation improved the triage quality for suspect skin lesions by 2.24-fold.

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**KEYWORDS**

melanoma, non-melanoma skin cancer, primary health care, public health, skin cancer, teledermatology, teledermoscopy

**INTRODUCTION**

The incidence of melanoma (MM) and non-melanoma skin cancer (NMSC) is steadily rising over years,<sup>1–3</sup> and leads to an increased workload for first-line healthcare professionals (FHPs) and dermatologists.<sup>4</sup> Furthermore, the dearth of dermatologists and long waiting times hamper rapid diagnosis and management, with potentially worse prognoses.<sup>4</sup> Triage in primary healthcare centres (PHCs) could be useful, but FHPs often lack faith in their clinical diagnoses.<sup>4</sup> Teledermoscopy (TDS), defined as dermatoscopic images that are analysed at distance using telecommunication technologies, may help to distinguish skin lesions and speed up the management of suspicious lesions.<sup>5</sup> Finally, in terms of public health, early diagnosis followed by appropriate management remains the cornerstone of reduced skin cancer morbidity and mortality.<sup>6</sup>

In 2019, a pilot TDS project (TELESPOT (TELEdermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce)) was conducted in six PHCs for a 1-year test period in the French-speaking part of Belgium.<sup>7</sup> In contrast to previous dermoscopy studies, the development of our system was based on open-source applications and programs. The main advantages of open-source development are flexibility, sustainability, security and reduced costs.<sup>8</sup> Our application was principally focused on distinguishing benign versus malignant lesions and on prioritising clinical management. After 1 year, the impact on skin cancer care of our TDS referral system was highly appreciated in all PHCs, in good agreement with results from previous reports. Patient and HCP satisfaction rates were not assessed in those studies.<sup>8</sup>

This article resumes the results of the final evaluation of the TELESPOT project after a period of 3 years.

**MATERIALS AND METHODS****Ethics**

This study was performed in accordance with the Helsinki Convention on Human Rights. The ethics committee and the university hospital legal department approved the project. The patients were informed about all the procedures and all signed the informed consent

forms, and authorised the electronic transfer of clinical data and images (Ethics Committee of the CHU, Sart Tilman (707), Avenue de l'Hôpital, Liège, B-4000, Belgium).

**Description of the patient care pathway**

The PHCs were trained to use the in-house developed system and associated smartphone application. An on-site basic training course reviewed the clinical and dermoscopic appearances of the major benign and malignant skin lesions.<sup>7,8</sup> Once a lesion was considered as suspect, macroscopic and dermoscopic images were acquired and sent for evaluation to a tertiary skin cancer centre (TSCC), rendering within 48 h a recommendation for a low- or high-priority management (LPM or HPM; Figure 1).

**Demographics**

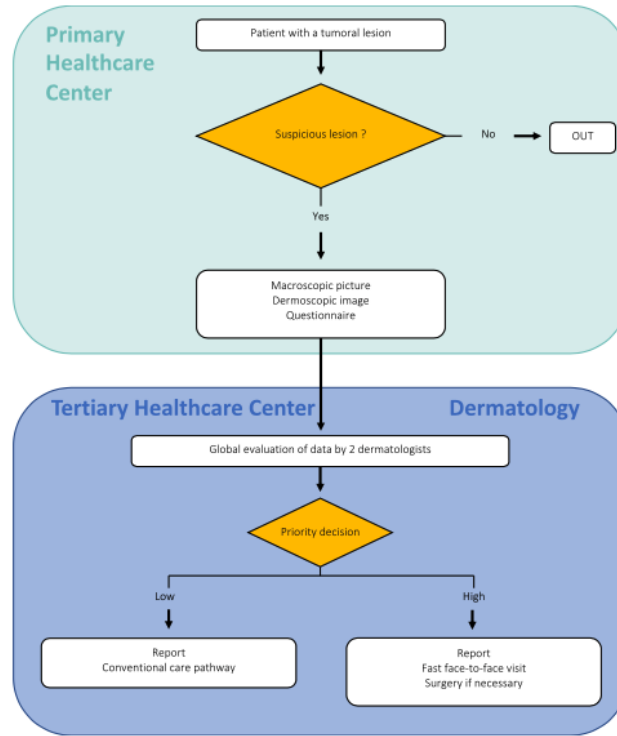
The following demographic data were recorded for each patient; age and gender, phototype, indoor versus outdoor profession and a personal and familial history of prior skin cancer. The TSCC report included a final diagnosis based on the demographic, macroscopic and dermoscopic images as well as a recommendation for LPM or HPM.

The initial period (phase 1) included acquisitions from six PHCs performed between September 2019 and August 2020. The extension period (phase 2) included data from the six initial PHCs and from three additional PHCs gathered between September 2020 and August 2022.

PHCs were considered as close (<20 km) or distant (≥20 km) to the TSCC and as medium size (<10 general practitioners [GPs]) or large (≥10 GPs). The mean age of the GPs, single or multiple TELESPOT users per PHC and the number of additional teaching visits to the PHCs were recorded.

**Outcomes**

Comparisons of endpoints were performed between different periods: group 1 = 6 initial PHCs in phase 1,



**FIGURE 1** Detailed TELESPOt pathway (see: Ref 8).

group 2 = 6 initial PHCs in phase 2, group 3 = 3 additional PHCs in phase 2 and group 4 = all 9 PHCs in phase 2.

The primary outcome was the number of LPM versus HPM recommendations between the four groups.

Secondary outcomes included the percentages of malignant skin lesions among all the recorded lesions, the quality of the acquisition (evaluable or not-evaluable), the mean time between the TSCC report and the surgery for HPM lesions in comparison with a conventional in-house care pathway (mean: 81 days), the correlation between the TSCC report for HPM lesions and their histopathological diagnosis, the localisation of the all the acquired lesions, the duration between the patient's awareness of the lesion and the actual acquisition in the PHC, the number of acquisitions by PHC per

season, as well as the patient and GP satisfaction scores, as previously defined. Wherever relevant, the secondary outcomes were compared between the four groups.

### Statistical methods

Results are presented as means and standard deviation (SD), quartiles (medians, Q1–Q3) and range (minimum–maximum) for quantitative variables and as frequency tables for qualitative variables. Descriptive statistics as well as comparison between diagnosis and histopathology for HPM lesions are provided on all lesions, in each phase and in each type of PHC in phase 2. The outcomes, that is, nature of the lesion, priority management, repetition and degree of certainty, were analysed

by a repeated logistic model (genmod) accounting for the fact that some PHCs are included in both phases. In the model, the type of PHC (initial PHCs or additional PHCs) and the study phase were considered as fixed effects and PHC as a random effect. Results are considered significant at the 5% uncertainty level ( $p < 0.05$ ). Analyses were performed using the SAS version 9.4.

## RESULTS

### Patient demographics

Out of the 335 patients, 56.4% were female (mean age: 50.5 years, min: 2, max: 94 years). The median phototype was 3 (min: 1, max: 6). A minority of patients had an outdoor profession (7.8%). A personal history of prior skin cancer was noted in 3% of the patients. Table 1 illustrates the patient demographics according to the four groups.

### PHC demographics

In phase 1, all the six enrolled PHCs were close to the TSCC and four of the six were considered as large size PHCs. In phase 2, the three additional PHCs were distant to the TSCC and all were considered as medium size PHCs. Individual data of the PHCs are presented in Table 2.

### Primary outcome

HPM was recommended in 9.2% of the 478 analysed lesions, corresponding to 13.1% of the total cohort of 335 patients. Table 3 details the comparison of triage among the four groups. The logistic regression model (genmod) with PHC as random effect and, study phase and type of PHC as fixed effects, shows that the probability of classifying a lesion as HPM is lower for additional PHCs ( $p = 0.023$ ). This probability tends to be higher in phase 2 than in phase 1 but not significant ( $p = 0.057$ ; Table 3).

**TABLE 1** Demographic data of 335 participation patients.

| Variable         | Categories | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|------------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|                  |            | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Sex              |            | 77                      |            | 84                      |            | 176                        |            | 259                 |            |
|                  | Female     | 52                      | (67.5)     | 45                      | (53.6)     | 92                         | (52.3)     | 137                 | (52.9)     |
|                  | Male       | 25                      | (32.5)     | 39                      | (46.4)     | 84                         | (47.7)     | 122                 | (47.1)     |
| Phototype        |            | 77                      |            | 84                      |            | 176                        |            | 259                 |            |
|                  | 1          | 3                       | (3.9)      | 3                       | (3.6)      | 2                          | (1.1)      | 5                   | (1.9)      |
|                  | 2          | 30                      | (39.0)     | 33                      | (39.3)     | 63                         | (35.8)     | 96                  | (37.1)     |
|                  | 3          | 22                      | (28.6)     | 24                      | (28.6)     | 102                        | (58.0)     | 125                 | (48.3)     |
|                  | 4          | 19                      | (24.7)     | 21                      | (25.0)     | 8                          | (4.5)      | 29                  | (11.2)     |
|                  | 5          | 1                       | (1.3)      | 2                       | (2.4)      | 1                          | (0.6)      | 3                   | (1.2)      |
|                  | 6          | 2                       | (2.6)      | 1                       | (1.2)      | 0                          | (0.0)      | 1                   | (0.4)      |
| Profession       |            | 77                      |            | 84                      |            | 176                        |            | 259                 |            |
|                  | Indoor     | 69                      | (89.6)     | 77                      | (91.7)     | 165                        | (93.8)     | 241                 | (93.1)     |
|                  | Outdoor    | 8                       | (10.4)     | 7                       | (8.3)      | 11                         | (6.3)      | 18                  | (6.9)      |
| Personal history |            | 77                      |            | 84                      |            | 176                        |            | 259                 |            |
|                  | No         | 75                      | (97.4)     | 80                      | (95.2)     | 172                        | (97.7)     | 251                 | (96.9)     |
|                  | Yes        | 2                       | (2.6)      | 4                       | (4.8)      | 4                          | (2.3)      | 8                   | (3.1)      |
| Familial history |            | 77                      |            | 84                      |            | 176                        |            | 259                 |            |
|                  | No         | 76                      | (98.7)     | 76                      | (90.5)     | 169                        | (96.0)     | 244                 | (94.2)     |
|                  | Yes        | 1                       | (1.3)      | 8                       | (9.5)      | 7                          | (4.0)      | 15                  | (5.8)      |

Abbreviation: PHC, primary healthcare centre.

**TABLE 2** PHCs demographic data.

|                                  | PHC 1    | PHC 2  | PHC 3    | PHC 4    | PHC 5    | PHC 6  | PHC 7  | PHC 8    | PHC 9    |
|----------------------------------|----------|--------|----------|----------|----------|--------|--------|----------|----------|
| Distance to tertiary centre (km) | 15       | 13     | 11       | 11       | 10       | 5      | 115    | 113      | 129      |
| Number of GPs                    | 12       | 4      | 12       | 9        | 13       | 35     | 6      | 7        | 5        |
| Mean age of GP (years)           | 43.3     | 38.7   | 45.4     | 41.6     | 44.3     | 48.2   | 44.8   | 40.9     | 37.8     |
| User mode                        | Multiple | Single | Multiple | Multiple | Multiple | Single | Single | Multiple | Multiple |
| Additional investigator visits   | 3        | 2      | 1        | 1        | 1        | 2      | 1      | 0        | 0        |

Abbreviations: GP, general practitioner, km, kilometre; PHC, primary healthcare centre.

**TABLE 3** Distribution of HPM versus LPM lesions.

| Variable            | All lesions |            | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|---------------------|-------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|                     | N           | Number (%) | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Management priority | 478         |            | 105                     |            | 115                     |            | 258                        |            | 373                 |            |
| Low                 |             | 434 (90.8) |                         | 97 (92.4)  |                         | 97 (84.3)  |                            | 240 (93.0) |                     | 337 (90.3) |
| High                |             | 44 (9.2)   |                         | 8 (7.6)    |                         | 18 (15.7)  |                            | 18 (7.0)   |                     | 36 (9.7)   |

Note: probability of classifying a lesion as HPM is lower for additional PHCs ( $p = 0.023$ ). This probability tends to be higher in phase 2 than in phase 1 but not significant ( $p = 0.057$ ).

Abbreviations: HPM, high-priority management; LPM, low-priority management; PHC, primary healthcare centre.

### Secondary outcomes

Of the 478 TSCC analysed lesions, 84.6% were classified as benign, 3.7% as uncertain and 11.7% as malignant. Table 4 details the comparisons between the four groups. The logistic regression model (genmod) with PHC as random effect and, study phase and type of PHC as fixed effects, reveals that the probability of classifying the lesion as malignant is not related to the type of site (initial PHCs or additional PHCs;  $p = 0.64$ ) nor to the phase ( $p = 0.071$ ) but there is a tendency. Indeed, the probability tends to be higher in phase 2 than in phase 1.

In global, 1.9% of the acquisitions were judged as non-evaluable and repetition of image acquisition was required. Table 5 details the comparison in the four groups. The logistic regression model (genmod) with PHC as random effect and, study phase and type of PHC as fixed effects, shows that the probability of a repeated acquisition is not related to the type of site ( $p = 0.14$ ) nor to the phase ( $p = 0.20$ ).

For the 44 HPM lesions, the mean interval between the TSCC report and surgery was 9 days.

Among the suggested TSCC diagnosis of the 44 HPM lesions, 37 (84.1%) were confirmed by histopathology. The TSCC proposed diagnoses of NMSC were all

**TABLE 4** Distribution of benign, malignant and uncertain classification.

| Variable             | All lesions |            | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|----------------------|-------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|                      | N           | Number (%) | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Nature of the lesion | 478         |            | 105                     |            | 115                     |            | 258                        |            | 373                 |            |
| Benign               |             | 405 (84.7) |                         | 91 (86.7)  |                         | 92 (80.0)  |                            | 222 (86.0) |                     | 314 (84.2) |
| Uncertain            |             | 18 (3.8)   |                         | 6 (5.7)    |                         | 7 (6.1)    |                            | 5 (1.9)    |                     | 12 (3.2)   |
| Malignant            |             | 55 (11.5)  |                         | 8 (7.6)    |                         | 16 (13.9)  |                            | 31 (12.0)  |                     | 47 (12.6)  |
| Benign+Uncertain     |             | 423 (88.5) |                         | 83 (92.4)  |                         | 99 (86.1)  |                            | 227 (88.0) |                     | 326 (87.4) |
| Malignant            |             | 55 (11.5)  |                         | 8 (7.6)    |                         | 16 (13.9)  |                            | 31 (12.0)  |                     | 47 (12.6)  |

Abbreviation: PHC, primary healthcare centre.

**TABLE 5** Distribution of repetition.

| Variable   | All lesions |            | Phase 1<br>Initial PHCs |            | Phase 2<br>Initial PHCs |            | Phase 2<br>Additional PHCs |            | Phase 2<br>All PHCs |            |
|------------|-------------|------------|-------------------------|------------|-------------------------|------------|----------------------------|------------|---------------------|------------|
|            | N           | Number (%) | N                       | Number (%) | N                       | Number (%) | N                          | Number (%) | N                   | Number (%) |
| Repetition | 478         |            | 105                     |            | 115                     |            | 258                        |            | 373                 |            |
| No         |             | 468 (97.9) |                         | 102 (97.1) |                         | 114 (99.1) |                            | 252 (97.7) |                     | 366 (98.1) |
| Yes        |             | 10 (2.1)   |                         | 3 (2.9)    |                         | 1 (0.9)    |                            | 6 (2.3)    |                     | 7 (1.9)    |

Abbreviation: PHC, primary healthcare centre.

confirmed by histopathology. Among the melanocytic lesions highly suspected of malignancy, 11 of the 18 (61.1%) were diagnosed as melanoma (6 in situ MM, 4 superficial spreading MM and 1 malignant lentigo). The positive predictive value of the TSCC report for HPM lesions was 83.3% (95% confidence interval: 68.6%–93.0%).

The anatomical distribution of all the lesions was as follows: head and neck ( $n = 102$ ; 21.3%), trunk ( $n = 102$ ;

21.3%), upper limbs ( $n = 81$ ; 16.9%), lower limbs ( $n = 54$ ; 11.3%) and genital area ( $n = 4$ ; 0.8%).

The distribution of the interval between the patient's awareness of the lesion and the actual acquisition were: <1 month ( $n = 53$ ; 11.1%), 1–3 months ( $n = 73$ ; 15.3%), 3–6 months ( $n = 46$ ; 9.6%), 6–12 months ( $n = 75$ ; 15.7%) and >12 months ( $n = 231$ ; 48.3%). The proportion of HPM lesions among these intervals were 9.4%, 10.3%, 11.6%, 11.7% and 6.5%, respectively.

**TABLE 6** Detailed GP and patient satisfaction scores.

|  | Phase 1<br>( $n = 6$ )                   | Phase 2<br>( $n = 20$ )                  |
|--|--|--|
| <b>GP satisfaction scores</b>  |  |  |
| The project easily fits into daily practice  | 8.6                                      | 8.9                                      |
| The acquisition technique is not very time-consuming                                     | 9.4                                      | 9.6                                      |
| Satisfaction with the report and advice  | 9.6                                      | 9.5                                      |
| The project accelerates diagnosis of suspicious skin lesions in my patients              | 9.0                                      | 9.1                                      |
| The project represents a health benefit for my patients                                  | 8.8                                      | 8.8                                      |
| Involvement in skin cancer screening   | 8.6                                      | 8.8                                      |
| Improving diagnostic competencies in distinguishing benign versus malignant skin lesions | 6.8                                      | 7.1                                      |
| More eager to do a complete skin check-up  | 7.6                                      | 7.2                                      |
| The project adds value to PHC  | 9.2                                      | 8.3                                      |
| Global satisfaction with the project   | 9.4                                      | 9.7                                      |
| <b>Patient satisfaction scores</b>   | <b>Phase 1<br/>(<math>n = 19</math>)</b> | <b>Phase 2<br/>(<math>n = 64</math>)</b> |
| Comfort with procedure   | 9.4                                      | 9.5                                      |
| Confidence about this new technology   | 8.6                                      | 8.7                                      |
| Trust in specialised advice  | 8.2                                      | 8.1                                      |
| Willingness to repeat the experience   | 8.8                                      | 9.0                                      |
| Global satisfaction with the project   | 8.8                                      | 8.9                                      |

Abbreviations: GP, general practitioner; PHC, primary healthcare centre.



The seasonal distribution of acquisitions was as follows: spring: 39.5%, summer: 27.6%, autumn: 13% and winter: 19.9%.

The global satisfaction score of GPs was 9.4/10 for the initial period and 9.7/10 for the extension period. The global satisfaction score of the patients was 8.8/10 and 8.9/10, respectively (Table 6).

## DISCUSSION

The pilot phase of the TELESPOOT project showed that this TDS system in PHCs represented a useful triage tool for suspicious skin lesions and permitted to adequately prioritise care management.<sup>8</sup> The extension phase consolidated the anterior results in a larger cohort and longer evaluation period.

In total, an HPM was recommended in 9.2% of the cases. The proportion of HPM was 7.6% during phase 1 versus 9.7% in phase 2. This could indicate a trend towards an improved triage in the PHCs, but this increase was not statistically significant. However, when evaluating the 6 PHCs who participated in both periods, there was a statistically significant improvement in triage (phase 2: 15.7% vs. phase 1: 7.0%; ratio = 2.24). Hence, the PHCs became more performant over time in discriminating the skin lesions.

These results are probably due to at least two factors: The 3-year participation in this project forced the GP to show interest in this type of lesions, probably improving his diagnostic capacities. Furthermore, the feedback of the diagnosis from the tertiary centre, however, without providing the GP with a dermoscopic description of the lesion, also helped them to improve their diagnostic skills. This is probably a type of cognitive intuitive learning process.

The clinical and/or dermoscopic images were judged as non-evaluable in 1.9% of the cases and a second acquisition of the lesion was required. This value lies between two other similar studies, reporting 0.4%<sup>9</sup> and 9.5% as non-evaluable.<sup>10</sup> There was no significant difference in percentages between the three additional PHCs compared to the 6 initial PHCs.

The mean interval between an HPM TSCC report and a visit (and surgery if needed) was 9 days, nine times faster in comparison with the conventional care pathway (median waiting time for a dermatology visit in Belgium: 81 days). This highly significant acceleration of management underlines the efficiency of the TDS system in the fight against skin cancer.

Out of all the lesions recommended for HPM, 84.1% were histopathologically confirmed. All lesions classified as NMSC were histopathologically confirmed. Among

the melanocytic lesions highly suspected of malignancy, 61.1% were histopathologically confirmed as MM with more than half (54.5%) as in situ MM. This fact could be explained by the sole participation in the project, increasing awareness, and maybe also by speeding up the delay between the diagnostic suspicion and the factual surgery. However, larger series and longer observations will be required to validate or not this fact. MM represented 2.3% of all analysed lesions and 25% of all the HPM lesions. These data are comparable to other studies.<sup>10</sup> The seven melanocytic lesions clinically and dermoscopically highly suspected of malignancy comprised, two Spitz nevi, one dysplastic naevus, two congenital nevi, one benign naevus and one seborrheic keratosis, as assessed by histology subsequently. Globally, the positive predictive value of the TSCC report for HPM lesions was 83.3% (95% confidence interval: 68.6%–93.0%).

In both periods, it was challenging to observe that 48.3% of the lesions sent in for advice were present for more than 12 months. Only 26.4% were present less than 3 months. No comparable data were available in the other studies.<sup>9,10</sup> This indicates that one out of two individuals are still not aware of the risks of skin cancer and that the sooner the diagnosis is made, the better the prognosis is. In contrast, the message about the link between sun exposure and skin cancer seems better known. Indeed, more than two out of three lesions were acquired during the spring and summer months.<sup>11,12</sup>

The GP and patient satisfaction scores were excellent and maintained stable between phases 1 and 2. These results are well in line with other studies reporting GPs and/or patient satisfaction levels.<sup>13–15</sup> The TDS system confirms its general usefulness, easy implementation and user-friendliness.

The main limitation of a TDS system still remains the initial triage in PHCs. Rare clinical presentations such as amelanotic melanoma are still easily missed.<sup>16</sup> A recent retrospective study compared the initial self-reported referral decisions of GPs before TDS system versus their final self-reported referral decisions after TDS system for skin lesions diagnosed by the teledermatologist (TD) as (pre)malignant or benign.<sup>17</sup> In half of the TDS consultations, GPs adjusted their initial referral decision after TD advice and TD diagnosis. Initially, GPs did not have the intention to refer 56.8% of patients with a malignant TDS diagnosis and 16.0% of patients with a premalignant TD diagnosis but then decided to refer these patients after the TDS consultation.<sup>17</sup> Moreover, GPs adjusted their decision from referral to nonreferral in 74.9% of benign skin lesions.<sup>17</sup>

Another limitation in the evaluation of the TELESPOOT project was to not include a control visit for LPM

lesions. However, the high sensitivity and specificity rates of TDS systems were already demonstrated.<sup>4,18</sup> These studies showed no significant difference in sensitivity between in vivo consultations versus TDS referrals, especially in distinguishing a benign versus malignant lesion<sup>18</sup>; the diagnostic accuracy for a primary diagnosis and benign versus malignant triage with TDS were 58.2% (95% CI, 52.3–63.9) and 80.1% (95% CI, 75.0–84.5), respectively. The TELESPOt design better reflects the final aim of TDS in real-life healthcare conditions: reducing unnecessary in vivo visits and accelerating the management of suspicious lesions. A final limitation could be that a TDS system is not fitted for a total body skin examination.<sup>19</sup>

In conclusion, this long-term evaluation indicates the added value of this TDS for PHCs, delivering a high GP and patient satisfaction, an efficient tool for an accelerated management of a suspect lesion and an effective triage as well as avoiding unnecessary patient travel and specialised care visits. In addition, this evaluation showed that long-term participation resulted in a 2.24-fold improved triage quality of the PHCs.

An eventual implementation in national healthcare systems of this kind of project will depend on a series of legal, medical, professional and technical regulations.

#### AUTHOR CONTRIBUTIONS

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, taking responsibility for the integrity of the work as a whole, and have all given their final approval for this version to be published. Thomas Damsin and Arjen F. Nikkels both provided significant contributions to the conception and design, the analysis and interpretation of the data and the drafting of the final article and revising it critically for important intellectual content, and the final approval of the version to be published. Gregory Canivet, Pauline Jacquemin, Laurence Seidel, Gilles Absil, Didier Giet and Pierre Gillet critically revised the intellectual content and approved the final version to be published.

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#### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

#### DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this published article as Supporting Information files.

#### ETHICS STATEMENT

This study was performed in accordance with the Helsinki Convention on Human Rights. The ethics committee and the university hospital legal department approved the project. All patients in this manuscript have given written informed consent for participation in the study and the use of their deidentified, anonymized, aggregated data and their case details for publication.

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## 1.2. Related publications as first author

1.2.1. Damsin T, Lebas E, Marchal N, Rorive A, Nikkels A. Cemiplimab for locally advanced and metastatic basal cell carcinoma. *Expert Rev Anticancer Ther.* 2022 Feb 17

1.2.2. Damsin T, Nikkels A (2022, April). TELESPOT Project, a Belgian teledermoscopy system in primary healthcare centers for skin cancer early detection : Prospective Preliminary Results and Satisfaction Evaluation. « European Association of Dermato-Oncology » 18<sup>th</sup> congress, Seville, Spain


**18<sup>TH</sup> EADO CONGRESS**  
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 APRIL 21<sup>ST</sup>-23<sup>RD</sup>  
ON SITE CONGRESS WITH ADDITIONAL VIRTUAL ACCESS

### TELESPOT Project, a Belgian teledermoscopy system in primary healthcare centres for skin cancer early detection : Prospective Preliminary Results and Satisfaction Evaluation

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**Introduction** The incidence of skin cancer has been steadily increasing for years<sup>1</sup>. This situation has led to a workload for primary healthcare centres (PHCs) and dermatologists, hampering early diagnosis and care<sup>2</sup>. Teledermoscopy allows standardized and reproducible cutaneous tumour image analysis with high sensitivity and specificity<sup>3</sup>. TELESPOT project (Teledermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce) provides rapid diagnosis and speed up patient flow (figure 1)<sup>4</sup>.

**Material and Methods**

**Smartphone Application Development** The data processing is made with open source program and the General Data Protection Regulation is respected.

**Smartphone Dermoscopic Device** a smartphone (iPod® Touch 7; Apple, Cupertino, CA) and a compatible handheld dermatoscope (Hein® ic; Heine Optotechnik, Hirsching, Germany) were provided to each PHC.

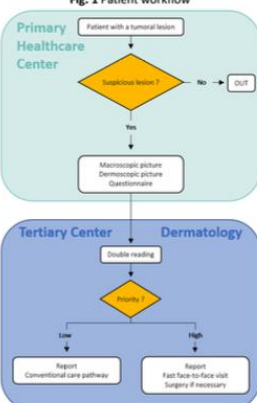
**Trainings of PHCs** Each PHC were aware to skin cancer demographic, clinical and dermoscopic features; trained to acquire macroscopic and dermoscopic pictures and fill questionnaire.

**Project Settings** 7 PHCs were enrolled, in 4 different french Belgian districts.

**Screening Items** Quality of acquisition, evolution of lesion over time, nature of lesion, diagnosis, management priority, histopathology of high priority lesions, time to face-to-face visit (and surgery if necessary) for high priority lesions.

**Satisfaction Scores** General practitioners (GPs) and patients satisfaction were assessed with a modified Likert scale.

**Fig. 1 Patient workflow**



**Fig. 2 Diagnostic categories**

| Diagnostic category                               | n = 325 (%) |
|---|-------------|
| Actinic keratosis                                 | 12 (3,7)    |
| Angioma   | 11 (3,8)    |
| Atypical nevus                                    | 9 (2,6)     |
| Basal cell carcinoma                              | 12 (3,7)    |
| Benign nevus                                      | 120 (36,9)  |
| Dermatofibroma                                    | 5 (1,5)     |
| Epidermoid carcinoma                              | 8 (2,5)     |
| Lentigo simplex                                   | 19 (5,8)    |
| Other benign lesions                              | 20 (6,1)    |
| Other malignant lesions                           | 1 (0,3)     |
| Seborrheic keratosis                              | 92 (28,3)   |
| Melanocytic lesion highly suspected of malignancy | 16 (4,8)    |
| - Congenital nevus                                | - 2 (0,6)   |
| - Spitz/Reed nevus                                | - 3 (0,9)   |
| - Dysplastic nevus                                | - 1 (0,3)   |
| - In situ melanoma                                | - 6 (1,8)   |
| - Superficial spreading melanoma                  | - 4 (1,2)   |

**Results**

**Satisfactions Scores** The overall satisfaction score was 9.4/10 for GPs and 8.8 for patients.

**Screening Results** We analysed 325 lesions from 227 patients (figure 2). Mean age was 51 years with a female dominance (3:2). 3% of acquired pictures must be repeated because of poor quality. Low priority management was advised for 88% of lesions. Melanoma represented 26% of high priority lesions. Median time to face-to-face visit (and surgery if needed) for high priority lesions was 12 days, that is seven times faster in comparison with conventional care pathway.

**Conclusion** The preliminary evaluation shows TELESPOT project as a useful tool to preselect patient with suspicious cutaneous lesion and provide rapid access to specialized care. One limitation to our system remains the initial triage by first-line medicine, which may miss uncommon cancer clinical presentation (e.g. amelanotic melanoma).

1. *Belgian Cancer Register (Belcar) - Center for an aging population - Belgium 2016-2018*. Brussels: Belgian Cancer Register; 2019. p. 65-74.

2. *Costa J, Kralovics V. Telemedicine: New horizon of practice in emerging techniques of the modern era*. 2017. [https://doi.org/10.1007/978-94-007-5844-9\\_10](https://doi.org/10.1007/978-94-007-5844-9_10)

3. *Stangorini P, Pignatelli B, Sforza R et al. Diagnostic accuracy and satisfaction assessment: telemedicine of 100 melanocytic lesions*. *Journal of Cutaneous Medicine and Surgery*. 2018; 24(10):1031-1035.

4. *Damsin T, Canivet G, Jacquemin P et al. Value of telemedicine in primary healthcare centers: preliminary results of the TELESPOT project*. *European Association of Dermato-Oncology*. 2022; 18(1):1-3.

1.2.3. Damsin T, Nikkels A (2022, September). *TELESPOT Project, a teledermatology tool for primary healthcare centers for early skin cancer diagnosis in Belgium: intermediate results and satisfaction scores.* « European Academy of Dermatology and Venereology » 31<sup>st</sup> congress, Milan, Italy



**TELESPOT Project, a teledermatology tool in primary healthcare centers for skin cancer early diagnosis in Belgium:**

Intermediate results and satisfaction scores

Damsin T, Canivet G, Jacquemin P, Seidel L, Gillet P, Giet D, Nikkels A.

**Introduction** The incidence of skin cancers has been steadily increasing for decades<sup>1</sup>. This situation has led to a higher workload for primary healthcare centers (PHCs) and dermatologists, hampering early diagnosis and management<sup>2</sup>. Standardized and reproducible skin tumour image analysis with high sensitivity and specificity is effective with teledermoscopy<sup>3</sup>. TELESPOT project (TELEdermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce) supplies rapid diagnosis and speeds up patient care flow (figure 1)<sup>4</sup>.

**Material and Methods**

**Project application development:** data processing was created with open source program. General Data Protection Regulation is followed.

**Handheld dermoscopic device:** each PHC is equipped with a smartphone (iPod® Touch 7; Apple, Cupertino, CA) and a compatible dermatoscope (Heine® ic1; Heine Optotechnik, Herrsching, Germany).

**Training of PHCs:** demographic, clinical and dermoscopic features of skin cancers were basically were taught to PHCs. Each centre was trained in macroscopic/dermoscopic images and survey acquisition.

**Project setting:** 7 PHCs were enrolled in 4 different Belgian districts.

**Screening items:** quality of acquisition, evolution of lesion over time, nature of lesion, diagnosis, management priority, histopathology of high priority lesions, time to face-to-face (and surgery if necessary) visit for high priority lesions.

**Satisfaction evaluation:** a modified Likert scale was used for the assessment of PHCs and patients.

**Results**

**Screening results:** 353 lesions were analysed from 241 patients (figure 2). Mean age was 51 years with a female sex ratio [3:2]. 3% of acquired images must be repeated because of poor quality. Low priority management was given for 89% of lesions. Melanoma represented 26% of high priority lesions pool. Median time to face-to-face/surgery visit was 12 days, seven time faster in comparison with conventional care pathway.

**Satisfaction evaluation:** the global satisfaction score was 8.8/10 for patients and 9.4/10 for PHCs.

**Fig. 2 Diagnostic categories**

| Diagnostic category                               | n=353 (%)  |
|---|------------|
| Actinic keratosis                                 | 15 (4,3)   |
| Angioma   | 12 (3,4)   |
| Atypical naevus                                   | 9 (2,6)    |
| Basal cell carcinoma                              | 12 (3,4)   |
| Benign nevus                                      | 134 (37,9) |
| Dermatofibroma                                    | 6 (1,7)    |
| Epidemioid carcinoma                              | 9 (2,6)    |
| Lentigo   | 19 (5,4)   |
| Other benign lesions                              | 22 (6,2)   |
| Seborrheic keratosis                              | 88 (24,7)  |
| Other malignant lesions                           | 1 (0,3)    |
| Melanocytic lesion highly suspected of malignancy | 16 (4,5)   |
| Congenital nevus                                  | 2 (0,6)    |
| Spitz/Reed nevus                                  | 3 (0,8)    |
| Dysplastic nevus                                  | 1 (0,3)    |
| In situ melanoma                                  | 6 (1,7)    |
| Superficial spreading melanoma                    | 4 (1,1)    |

**Fig. 1 Patient workflow**

**Conclusion**

TELESPOT project claims to be a useful tool to pre-screen patient with suspicious skin lesion and speed up patient care management in this intermediate evaluation. The initial triage in PHCs might be a limitation to our project, missing uncommon skin cancer clinical manifestation such as amelanotic melanoma.

1. Belgian Cancer Registry Group. Cancer in an ageing population: Belgium 2004-2016. Brussels: Belgian Cancer Registry; 2018. p. 65-74.  
2. Coates S, Weedar J, Grandstein R. Teledermatology: from historical perspective to emerging techniques of the modern era, part 1: history, rationale and current practice. J Am Acad Dermatol. 2015;72(4):563-74.  
3. Veiergaard T, Priedel S, Schuster A et al. Diagnostic accuracy and interobserver concordance: teledermoscopy of 600 suspicious skin lesions in Southern Denmark. J Eur Acad Dermatol Venereol. 2020. http://doi.org/10.1111/jdv.16575.  
4. Damsin T, Canivet G, Jacquemin P et al. Value of teledermatology in primary healthcare centers: preliminary results of the TELESPOT project in Belgium. Dermatol Ther (Heidebl). 2020;10:1405-13.

1.2.4. Damsin T, Nikkels A (2022, December) Le projet Telespot, détection précoce des cancers cutanés par télédermoscopie en Médecine générale : premiers résultats et scores de satisfaction. Journées Dermatologiques de Paris 2022, Paris, France

## Le projet Telespot, détection précoce des cancers cutanés par télédermoscopie en Médecine générale : premiers résultats et scores de satisfaction

Damsin Th, Nikkels AF

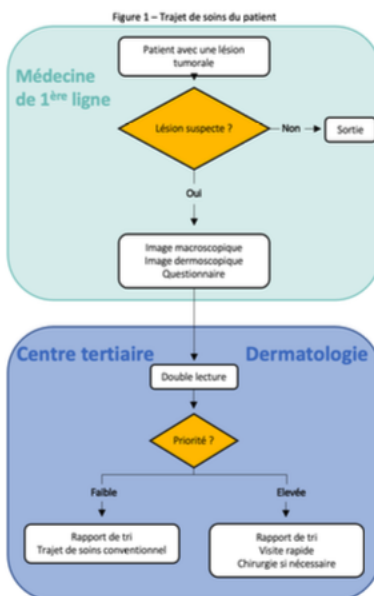
Service de Dermatologie, Centre Hospitalier Universitaire du Sart-Tilman, Liège (Belgique)

**Introduction** L'incidence des cancers cutanés est en nette et constante augmentation depuis des années<sup>1</sup>. Cette situation amène une charge de travail importante, tant en Médecine de première ligne que pour les dermatologues, entravant un diagnostic précoce et une prise en charge rapide<sup>2</sup>. La télédermoscopie permet une analyse sensible, standardisée et reproductible des tumeurs cutanées<sup>3</sup>. Le projet Telespot, acronyme de *Teledermoscopy Smartphone-based Pigmented lesion diagnosis Online Taskforce*, a pour objectif de fournir une aide diagnostique rapide et fiable dans le tri des lésions cutanées et d'accélérer la prise en charge des lésions suspectes (figure 1<sup>4</sup>).

**Matériel et méthodes** L'application a été développée à partir de programmes *open source*, dans le respect du Règlement Général sur la Protection des Données. Chaque centre de soins primaires est équipé d'un smartphone (iPod® Touch 7; Apple, Cupertino, CA) et d'un dermatoscope compatible (Heine® ic1; Heine Optotechnik, Herrsching, Germany). Les sept centres participants ont reçu une formation de base sur les caractéristiques démographiques, cliniques et dermoscopiques des tumeurs cutanées.

Les paramètres suivants ont été analysés : qualité de l'acquisition, délai de progression de la lésion, nature de la lésion, proposition diagnostique, priorité de prise en charge, analyse histopathologique des lésions à priorité élevée, délai entre le rapport de tri et la prise en charge du patient. L'évaluation de la satisfaction des centres de soins primaires participants et des patients a été réalisée via une échelle de Likert modifiée.

**Résultats** 408 lésions ont été analysées chez 284 patients (figure 2) avec une moyenne d'âge de 51 ans et une tendance féminine (3:2). En terme de qualité d'acquisition, 3% des images enregistrées ont nécessité une nouvelle acquisition afin de répondre aux critères de qualité exigés. Une priorité faible de prise en charge a été donnée pour 89% des lésions. Les mélanomes représentent 30% des lésions à priorité élevée. Le délai entre le rapport de tri et la prise en charge de ces lésions à priorité élevée est de douze jours, soit une accélération du trajet de soins du patient d'un facteur sept par rapport au trajet conventionnel actuel. Le score de satisfaction général du patient et du centre de Médecine de première ligne est respectivement de 8,8 sur 10 et 9,4 sur 10.



| Catégorie diagnostique                                  | n = 408 (%) |
|---|-------------|
| Kératose actinique                                      | 16 (4,0)    |
| Angiome   | 12 (2,8)    |
| Naevus atypique   | 9 (2,3)     |
| Carcinome basocellulaire                                | 15 (3,8)    |
| Naevus bénin  | 158 (38,7)  |
| Dermatofibrome  | 6 (1,4)     |
| Carcinome spinocellulaire                               | 12 (2,8)    |
| Lentigo   | 23 (5,7)    |
| Autres lésions bénignes                                 | 23 (5,7)    |
| Autres lésions malignes                                 | 1 (0,2)     |
| Kératose séborrhéique                                   | 115 (28,2)  |
| Lésions mélanocytaires hautement suspectes de malignité | 18 (4,4)    |
| - Naevus congénital                                     | - 2 (0,5)   |
| - Naevus de Reed et de Spitz                            | - 3 (0,7)   |
| - Naevus dysplasique                                    | - 1 (0,2)   |
| - Mélanome in situ                                      | - 7 (1,8)   |
| - Mélanome superficiel extensif                         | - 4 (1,0)   |
| - Mélanome de type lentigo malin                        | - 1 (0,2)   |

Figure 2 – Catégories diagnostiques

**Conclusion** Le projet Telespot s'inscrit progressivement comme un outil utile et fiable en termes de tri des lésions cutanées et d'accès à une prise en charge rapide des lésions hautement suspectes de malignité. Une des limites de ce projet est le tri initial réalisé en Médecine de première ligne pouvant ignorer certaines présentations plus rares de cancers cutanés comme les mélanomes achromiques. Une évaluation au long cours de ce système de télédermoscopie permettra de mieux définir sa place dans la lutte contre les cancers cutanés.

1. Belgian Cancer Registry Group. Cancer in an ageing population: Belgium 2004-2016. Brussels: Belgian Cancer Registry; 2018. p. 65-74
2. Coates S, Kvedar J, Grandstein R. Teledermatology: from historical perspective to emerging techniques of the modern era, part I: history, rationale and current practice. *J Am Acad Dermatol*. 2015;72(4):563-74
3. Vestergaard T, Prasad S, Schuster A et al. Diagnostic accuracy and interobserver concordance: teledermoscopy of 600 suspicious skin lesions in Southern Denmark. *J Eur Acad Dermatol Venerol*. 2020. <http://doi.org/10.1111/jdv.16575>
4. Damsin T, Canivet G, Jacquemin P et al. Value of teledermatology in primary healthcare centers: preliminary results of the TELESPOt project in Belgium. *Dermatol Ther (Heidelb)*. 2020;10:1405-13

### 1.3. Related publications as co-author

1.3.1. *Absil G, Damsin T, Lebas E, et al. Melanoma : the patient's care pathway, from diagnosis to therapy. Rev Med Liege. 2021 May;76(5-6):489-495*

1.3.2. *Gedeah C., Damsin T., Absil G., et al. The impact of COVID-19 on the new diagnoses of melanoma. Eur J Dermatol 31(4), 565-567 (2021)*

1.3.3. *Absil G, Collins P, Seidel L, Damsin T, Nikkels. Clinical Features and Survival of Multiple Primary Melanoma: A Belgian Single Center Cohort. Dermatol Ther (Heidelb) 13, 641–649 (2023)*

## 2. Other publications

### 2.1. Other publications as first author

2.1.1. *Damsin T, Libon F, Nikkels AF, Dezfoulian B. Atopic dermatitis : the therapeutic revolution is underway. Rev Med Liege. 2022 May;77(5-6):377-383*

2.1.2. *Damsin T, Delahaye T, Dezfoulian B, Nikkels A (2023, March). Acute pancreatitis induced by topical isotretinoin: an unprecedented association. Belgian Dermatology Days 2023, Bruges, Belgium*

2.1.3. *Damsin T. A Case of Concurrent Psoriasis and Hidradenitis Suppurativa Successfully Treated with Tildrakizumab. Dermatol Ther (Heidelb). 2023 Jul;13(7):1611-1615*

### 2.2. Other publications as co-author

2.2.1. *Jouret G, Damsin T, Vanhakendover L et al. Dermatological manifestations of COVID-19. Rev Med Liege. 2020 Sup;75(S1):115-118*

2.2.2. *De Greef A, Ghislain PD, Bulinckx A, et al.. Real-Life Experience of Tralokinumab for the Treatment of Adult Patients with Severe Atopic Dermatitis: A Multicentric Prospective Study. Clin Drug Investig. 2023 Apr;43(4):299-306*

## Curriculum vitae

Doctor Thomas Damsin was born on October 5, 1992, and started his academic journey in medicine. He completed his MD degree in 2017 with the highest honors at the University of Liège in Belgium. This milestone marked his inception of professional commitment to the medical field.

Subsequently, Doctor Thomas Damsin started his dermatology residency program in 2017, a journey that would culminate in 2022 with yet another achievement of summa cum laude. During this intensive period of training, in 2020, he also earned the interuniversity degree in "Dermatological Manifestations of Systemic Diseases" at the University of Montpellier in France. This experience broadened his understanding of the intricate interplay between dermatology and systemic health, adding a valuable dimension to his expertise.

Upon completing his residency, he made the decision to remain within the university hospital environment, assuming the role of adjoint head of clinic under the benevolent supervision of Professor Arjen F. Nikkels. This position allowed him to further contribute to the field of dermatology, both in clinical practice, research and education. In his clinical practice, he focuses on inflammatory skin diseases, taking care of both outpatients and inpatients. He regularly collaborates with other internal medicine departments, such as rheumatology and gastroenterology. He is also actively involved in clinical trials conducted within the university department. This university environment also enables him to develop teaching skills with medical students, as well as those from other faculties such as pharmacy. On the scientific front, apart from writing directly for his thesis, he has written articles on various subjects. Finally, as both a participant and a speaker, he has attended several national and international conferences.