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### A NEW HEAD HOLDER AND TARGETING DEVICE FOR FRAMELESS STEREOTACTIC BRACHYTHERAPY OF THE HEAD AND NECK

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**Background&Purpose:** Accurate localization of the target is essential for brachytherapy of head and neck tumors. We have developed the VBH (Vogele-Bale-Hohner) head holder permitting rigid, non-invasive fixation of the head by using an individualized dental cast attached to the upper jaw by vacuum. The modified head holder in combination with a targeting device allows application of frameless stereotactic systems for accurate targeting of head and neck tumours.

**Material&Methods:** The modified VBH head holder consists of a plexiglass base plate, a headrest, three hydraulic arms, a mouthpiece (MP) and a counter-support. The hydraulic arms are attached to the base plate and connect to the counter-support and to the MP rod. Carbonfibre rods, indexed with fiducials, are mounted to the MP. The head is clamped between the dental impression and the counter-support in the parietooccipital region. For the scan the patient's head is immobilized in the head holder. A three-dimensional reconstruction is created. Needle entrance point and target are now defined. For the simulation process the hydraulic arms with the MP are repositioned and the virtual patient is registered by using the fiducials on the registration rods. During simulation, the targeting device is adjusted and the direction and length of the needle is determined. The patient and the targeting device are repositioned and brachytherapy is initiated.

**Results:** Our device allows accurate targeting of different structures of the head and neck. Repeated brachytherapy is possible without a need for additional CT- scans.

**Conclusion:** We present a new fixation and targeting device for brachytherapy of the head and neck with many advantages over conventional invasive fixation techniques.

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### DOES PROLIFERATION STATUS PREDICT RADIATION RESPONSE IN HUMAN TUMORS ?

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Tumor proliferative status (PS) may be an important prognostic indicator in human cancer of various origins. However, many questions related to PS remain unanswered. What is the best way to assess PS? Different assays are currently available: DNA ploidy and/or Tpot measurements after bromo- or iododeoxyuridine pulse labelling assessed by flow cytometry, assessment of mitotic index on histological slides, or silver staining of argyrophylic nucleolar organizer regions (AgNOR), or monoclonal antibodies against proliferation-associated nuclear antigens such as PCNA (PC10), p105 and Ki67/MIB-1, the comet/etoposide assay, and p53. All these tests have technical limits, and to date there are no firm data to state that there is an unambiguous correlation between tumor PS and treatment outcome in human tumors.

On the other hand, we are overwhelmed by an «avalanche» of clinical data pointing to the problem of treatment duration and outcome in radiation therapy. What are the limitations of these published restrospective studies? Are there prospective studies available attempting to answer the question of importance of treatment duration? Are there efforts to relate PS before treatment with outcome in a prospective manner and in well defined population of patients treated with « standard » radiation therapy? Most of available published data are hampered by a limited number of patients, a rather short follow-up, and lack of quality control of PS assessment. Considerable collaborative prospective efforts combined to extensive interlaboratory quality control of the technical factors in performing estimation of PS will be required. Quality control should allow to define if the measurement of pretreatment PS can be considered sufficiently reliable and reproducible as a possible predictive assay to be evaluated in current clinical practice.

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### DOES OXYGEN STATUS PREDICT RADIATION RESPONSE IN HUMAN TUMORS?

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It is well known that hypoxic tumor cells are relatively radiation resistant. Identification of hypoxia in human tumors has mainly been performed by the use of polarographic oxygen sensitive needle electrodes with the aim to evaluate the predictive value of pretreatment oxygenation status. The earliest oxygen electrodes for clinical use were glass sealed, slow reacting and measured superficially in the tissue of interest. Later technical improvement made computerized, faster responding steel covered electrodes available and now the method became clinically feasible. Several studies of $pO_2$ measurements in human tumors and normal tissues have been conducted. In spite of differences in histopathology, tumor site and the fact that technically different methods have been used, data are fairly consistent. Thus, the oxygenation status of normal tissue is in general significantly higher than in human tumors. However, a large variation in oxygenation status between tumors is evident and in some cases the oxygenation status of a tumor can be as well oxygenated as that of a normal tissue. Also intratumor heterogeneity is typical, but there is agreement between several reports that the variation between tumors is larger than the variation within tumors. More studies, are now available comparing pretreatment tumor oxygenation and treatment response. Apart from one case in soft tissue sarcomas most of these reports were performed in squamous cell carcinoma of the uterine cervix and head and neck. Several treatment modalities were used and the choice of treatment and oxygenation endpoints were heterogenous. Hypoxia was present in some tumors that reached local control as well as in tumors that failed, and tumors classified as nonhypoxic did not reach a 100% local control. Still, conclusions are similar and goes in favor of the hypothesis that presence of hypoxia in human tumors corresponds with excess risk of treatment failure and poor prognosis. So - yes oxygenation status does predicts radiation response in human tumors.

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### CAN INTRINSIC RADIOSENSITIVITY PREDICT RESPONSE TO THERAPY ?

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A number of groups have evaluated the ability of *in vitro* measurements of tumour intrinsic radiosensitivity to predict response to radiotherapy. Although many of the studies are too small to enable firm conclusions, the majority do show that radiosensitive tumours have, on average, a significantly better prognosis than radioresistant tumours. Where cell lines have been established prior to assessing radiosensitivity, no group has shown any correlation between tumour radiosensitivity and treatment outcome. The two largest studies have been carried out in Manchester and Paris and these have utilised a soft agar clonogenic assay and the CAM assay, respectively. Both have shown a significant relationship between radiosensitivity measured *in vitro* and patient response to radiotherapy. In Manchester data are available for 128 patients who received radiotherapy alone with a minimum 2 year follow-up. Pre-treatment measurements of surviving fraction at 2 Gy were highly prognostic for both local control and overall survival. Therefore, a review of the available clinical data suggests that tumour radiosensitivity is predictive for treatment outcome.