

News release – May 3, 2021

BioXmark® can provide a fast and reliable option for intraoperative marking of tumor resection surface in oral cancer patients

A publication from Steybe and colleagues from Medical Center – University of Freiburg, Germany on BioXmark® concludes:

- **Comparable or better visibility in CT and CBCT than titanium clips, even for markers of 10µl**
- **Improved delineation of 3D resection surface via injection of a high number of markers**
- **Good visibility on MRI for markers of a volume $\geq 50 \mu\text{l}$**

DK-Copenhagen – Nanovi informs about the results of a non-clinical study to evaluate BioXmark® for intraoperative marking of tumor resection surface in oral cancer patients. Such marking can facilitate precise postoperative delineation of the interface between the tumor resection border and the reconstructed tissue for Intensity Modulated Radiation Therapy (IMRT) and higher treatment accuracy.

The study was published by David Steybe et al. from Medical Center - University of Freiburg in Germany.

Study background and design

IMRT can increase the accuracy of radiation therapy (RT) for increased local tumor control and at the same time reduce the dose delivered to surrounding healthy tissue. In order to fully utilize the advantages of IMRT, a precise orientation of the interface between the tumor resection border and native/reconstructed tissue is paramount.

It has been demonstrated, that implanting titanium surgical clips is a feasible approach for postoperative identification of the tumor resection surface in oral cancer patients as well. However, marking the resection area with titanium clips has shortcomings, such as potential loss if the clips are placed superficially or migration of the clips. Migration of metallic clips may potentially reduce the accuracy of the marking procedure and artifacts from metal-based markers might impair their identification on post-operative imaging.

BioXmark® has been reported to provide a fast and reliable alternative for the creation of fiducial markers making it possible also to place a high number of markers to more accurately identify the resection surface.

The aims of this non-clinical study were:

- Evaluate the feasibility of the marking procedure with BioXmark®
- Assess the visibility of BioXmark® in CT, CBCT and MRI and quantify the correlation between the injected volumes of the resulting markers by threshold-based segmentation of the marker volume in CT- and CBCT imaging.

In order to evaluate the marking procedure of the soft tissue resection surface in oral cancer, BioXmark® was injected at a depth of 1-2 mm into the soft tissue of porcine mandible segments, using 25 G cannula.

To assess the marker visibility in CT, CBCT and MRI, a total of 200 markers with different volumes of 10µl, 20µl, 30µl, 40µl and 50µl were injected into the oral soft tissue of porcine mandible segments. Quantitatively analysis of the markers was performed by threshold-based segmentation procedure in CT and CBCT imaging. Moreover, a comparison between BioXmarks' and titanium clips' visibility was made. A comparison of signal intensities was performed to analyze the markers' visibility in T1W MRI imaging modality.

Results and conclusions

Feasibility

The technical feasibility of the marking procedure in oral soft-tissue resection surfaces using BioXmark was demonstrated. *"This technique was found to allow for the simple creation of a high number of radiopaque and MRI-visible markers within a short period of time."*

Visibility in CT and CBCT

Even the lowest volume of BioXmark® markers investigated (10µl) resulted in a higher segmentable volume than observed with the incorporation of titanium clips, thus proving excellent visibility.

Visibility in MRI

Due to its composition, the marker appears as hypointense structure (signal void) on MRI, making identification more difficult in this modality. The publication states: *"However, the ratio between the signal intensity of the marker and the signal intensity of the surrounding tissue showed a decrease with increasing injection volumes, resulting in 67.5% of the 50 µl injections providing good visibility in MRT1."*

These findings on MRI visibility are in accordance with the literature: Detectability of the individual marker deposits on T1W and T2W imaging has been described as being challenging without information from the corresponding CT-images due to signal voids from tissue heterogeneity or air cavities.

The publication concludes as follows:

- BioXmark® "provides a fast and reliable way to intraoperatively mark the tumor resection surface in oral cancer patients"



- "Injection volumes as low as 10 µl result in markers with a visibility comparable to the visibility of titanium ligature clips in CT and CBCT." CT imaging represents the standard in oral cancer RT planning
- MRI can provide valuable additional information however for MRI visibility higher volumes of BioXmark® should be injected (≥ 50 µl).
- The improvements in the marking procedure demonstrated by the results obtained in this investigation of BioXmark® will help considerably in adjuvant RT of oral cancer patients.
- BioXmark® might also help to identify local structural changes of the tumor resection surface, potentially due to tumor recurrency, by fusion of CT images acquired during the follow-up course.

Reference to the publication:

Steybe D, Russe MF, Ludwig U, Sprave T, Vach K, Semper-Hogg W, Schmelzeisen R, Voss PJ, Poxleitner P. Intraoperative marking of the tumour resection surface for improved radiation therapy planning in head and neck cancer: preclinical evaluation of a novel liquid fiducial marker. Dentomaxillofacial Radiology. 2020 Mar 1;50(3):20200290.

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About Nanovi

Nanovi A/S is a Danish medical device company specialized in precision marking for better cancer therapy. Our corporate dedication is to empower healthcare professionals with the best possible tools to expand their options for the delivery of high precision radiation therapy and surgery for the benefit of cancer patients and for healthcare efficiency.

Nanovi has a portfolio of unique in-house developed liquid fiducial markers for both human and veterinary use.

All our products are derived from a patented biomaterial technology system, co-invented with and licensed from the Department of Health Technology at the Technical University of Denmark, DTU.

For more information, please visit: www.nanovi.com