Press release

BioXmark® improves target delineation and is suitable for Small Animal Image-Guided Radiation Therapy (SAIGRT)

A recent publication of a study on BioXmark®, Nanovi's liquid fiducial marker, concludes:

- **Good marker safety, visibility and stability *in vivo***
- **Significantly lower CBCT imaging artifacts compared to solid fiducial markers**
- **Potential to align SAIGRT protocols for better animal welfare in research**

DK-Copenhagen, 14 September 2020 – Nanovi informs about the publication of a study, which compared image contrast performance and artifacts of BioXmark® with that of currently used solid fiducial markers for preclinical Cone Beam CT (CBCT) imaging applications. The study also evaluated the *in vivo* stability of BioXmark® and its impact on tumor radiation response.

The study was published by Kathryn Brown and colleagues from the Patrick G. Johnston Centre for Cancer Research at Queen's University Belfast in the field of Small Animal Image-Guided Radiation Therapy (SAIGRT) that is the current state-of-the-art in experimental radiation biology. SAIGRT enables previously unachievable approaches in preclinical radiation research and allows close mimicking of clinical exposure scenarios for further understanding of tumor and normal tissue radiation responses. The use of onboard CBCT imaging to deliver volumetric imaging of soft tissues is however, challenging in small animals. The use of fiducial markers for more precise target delineation can help to overcome these challenges for improved animal welfare, and the study was supported by the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).

BioXmark® is a novel liquid fiducial marker, developed and marketed by Nanovi, for use to enhance target visibility on imaging and enable high-precision radiation therapy across different cancer types.

Study background and design

The publication introduces the study as follows:

"Radiotherapy is a major modality in the radical treatment of cancer, being prescribed to >50% of patients during their treatment. In recent decades, significant advances in radiation therapy technology have enabled increasingly sophisticated, conformal delivery methods to be implemented into routine clinical practice".

This study compared artifacts on CBCT imaging of BioXmark® and of two solid fiducial markers, using phantom image analysis. *In vivo* stability with regard to both volume and migration of BioXmark® markers were evaluated with CBCT imaging analyses over a 5-month period in a mouse model. The study also evaluated the impact of BioXmark® markers on *in vivo* tumor radiation response in 48 mice with Lewis lung carcinoma, using a randomized controlled design.

Results and conclusions

In the phantom part of the study, BioXmark® markers were detectable on CBCT at volumes 10-60 µL. It was also shown that BioXmark® produced 89% and 84% lower imaging artifacts compared to solid gold- and polymer-based markers, respectively, which was significant. Reducing CBCT imaging artifacts may lead to improved segmentation and less uncertainty during radiation dose calculation.

In a mouse model, all injected volumes of BioXmark® were shown to be safe and well-tolerated. The markers were positionally stable with minimal migration from the injection site and no significant degradation for up to 5 months. The results support the use of this liquid fiducial marker in preclinical radiation therapy studies.

In a mouse tumor model, the effect of BioXmark® on tumor response *in vivo* from both single and fractionated radiation exposures was evaluated. BioXmark® had no significant impact on tumor growth in the control group. After a single fraction radiation, BioXmark® injected animals showed an equal tumor growth delay compared to the control group, indicating no adverse effect of BioXmark® on dose delivery. In the fractionated treatment setting, the delivered radiation dose was reduced due to artifacts by BioXmark® affecting the dose calculation. This could however, be mitigated by taking the impact into account in the treatment planning, leading to an even dose distribution to the tumors marked with BioXmark® compared to the control group.

The publication concludes that BioXmark® is a useful tool for improving target delineation and align protocols in SAIGRT studies withing the NC3Rs framework.

Reference to the publication:
Brown KH, Ghita M, Schettino G, Prise KM, Butterworth KT. Evaluation of a Novel Liquid Fiducial Marker, BioXmark®, for Small Animal Image-Guided Radiotherapy Applications. Cancers (Basel). 2020 May 18;12(5):1276. doi: 10.3390/cancers12051276.

Nanovi contact:

Jesper Boysen, CEO
Phone: +45 24 65 60 33
E-mail: jb@nanovi.com

About BioXmark®

BioXmark® is a liquid fiducial marker, developed by Nanovi for use to radiographically mark soft tissue and enable high precision radiation therapy across cancer types.

BioXmark® has the following features and benefits:

- *Liquid nature* for customizable implantation
- *Sticky and soft markers containing a proprietary contrast agent* for positional stability and visibility on relevant imaging modalities, including MRI
- *Non-metallic* for a low level of artefacts and low dose perturbation ensuring photon and proton compatibility

BioXmark® offers radiation therapy workflow benefits in the form of

- A fast and easy implantation procedure
- Less risk for procedure related complications
- No need for additional training nor special equipment

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 support the delivery of high precision radiation therapy and surgery for the benefit of cancer patients and for healthcare efficiency.

We have 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 platform, co-invented with the Department of Health Technology at the Technical University of Denmark, DTU.

The company's corporate offices are situated in Kgs. Lyngby, north of Copenhagen.

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