system. In this study, we investigate the targeting accuracy and throughput between the off- and on-line BLT setups.

Materials and Methods: For both on- and off-line BLT system, a three-mirror system was employed to direct the bioluminescence emitted from the mouse surface to a CCD camera. Four filters were used to acquire multispectral bioluminescence images for BLT reconstruction. CBCT was used to provide anatomical information for mesh generation used for BLT reconstruction. A 0.9 mm x 2 mm luminescence source was implanted in the abdomen of the mouse through surgical operation. The mouse was kept anesthetized with isoflurane during the whole experiment. With a high precision portable mouse bed for animal transport and image registration between the CBCT and BLT system, each mouse was transported and imaged on-board the SARRP and with the offline system in sequence. To evaluate the inter-setup error between the on-board and offline systems, we registered the CBCT images from the two systems and calculated the correlation between the images. In terms of assessing the accuracy of target localization, we devised the following test scenario: source reconstruction based on (1) on-board SARRP BLT and CBCT, (2) offline BLT and CBCT, and (3) reconstruction based on offline BLT and SARRP CBCT. The 3rd scenario examines the necessity of on-board optical imaging if a robust animal transport can be provided.

Results: Our results show the correlation coefficient between the mouse CBCTs acquired on board the SARRP and offline to be larger than 0.95 if a stable animal bed can be provided for transportation. The reconstructed center of mass (CoM) of the luminescence source is within 1 mm of the true CoM determined by CBCT for all 3 scenarios.

Conclusions: Our *in vivo* results demonstrate that if the setup error can be minimized between the offline BLT and SARRP, the off-line system can provide comparable accuracy to that of on-board BLT system. By allowing parallel BLT imaging and irradiation, the throughput can be substantially improved using an off-line BLT to localize the target for irradiation with the SARRP.

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Characterization of superparamagnetic, oxygen loaded NanoBubbles for hyperthermia and radiotherapy

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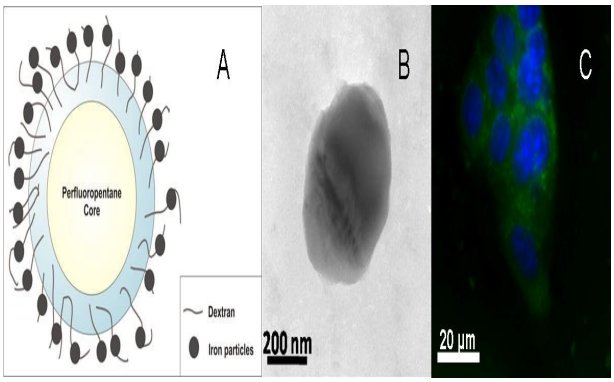
Purpose/Objective: Oxygen-loaded NanoBubbles (NBs) are attractive for their potential ability to enhance radiotherapy. In addition, functionalizing a nanocarrier with super-paramagnetic nanoparticles may generate a new specific, small sized and locally effective hyperthermic agent.

Materials and Methods: Superparamagnetic iron oxide nanoparticles (NPs) with a mean size of 30 nm were prepared using controlled co-precipitation. Phospholipids and palmitic acid were added under stirring to perfluoropentane and water at room temperature until the formation of an emulsion. Thereafter, the solution was saturated with O_2 and 1% dextran was added drop-wise to form the NB polymeric shell. Finally, 1 mg/ml of NPs were added to the suspension of NBs to interact electrostatically with the shell (Figure 1A). For fluorescence studies, 6-coumarin flourochrome was loaded to the NB formulation upon direct addition to perfluoropentane. Mean diameter was determined by Photo-Correlation Spectroscopy; for Z-potential determination, NB samples were placed in a electrophoretic cell. NBs morphology was observed by Scansion and Transmission Electron Microscopy (SEM and TEM; Figure 1B). Physical stability of the NBs was evaluated by measuring size and morphology over time. Hyperthermia measurements were obtained by means of an AC commercial applicator 'nanoScale Biomagnetics DM100'. The temperature increase was measured with an optical fiber thermometer to avoid the coupling with the RF field. NBs at a concentration of 1 or 2 mg/ml were irradiated for 10 min with a magnetic field of 250 Oe, 429 kHz for a SAR of 7.5 W/g. The NB uptake assay was performed on TUBO cells, a rat Her2/neu+ breast cancer cell line cultured in high glucose Dulbecco's Modified Eagle Medium with 1 % penicillin-streptomycin. TUBO cells were incubated for 24 h with/without 6-coumarin-labeled NBs in a humidified CO_2/air-incubator at 37°C. After DAPI staining to visualize cells nuclei, images were acquired by fluorescence microscope.

Results: NPs had an average diameter of about 30 nm and a Z-potential of +8.88 mV. The presence of NPs on the shell of NBs was verified using SEM. Moreover, the suspension was homogeneous and stable over three months. NBs appeared with an average diameter of 391.4 ± 35.8 nm and a Z-potential of -19.72 ± 1.24 mV.

Under RF exposure, we attained an additional heating from room temperature of 1.2 °C / 10 min for the 1 mg/mL NBs and of 1.8 °C/10 min for the 2 mg/mL NBs.

In the biologic experiment, NBs were avidly internalized by TUBO cells and were localized only in the cytoplasm compartment (Figure 1C).



Conclusions: We completely characterized superpara-magnetic, oxygen loaded NBs from preparation to heating potential and internalization skills in a cancer cellular model. Our NBs might be a new interesting tool for multifaceted tumor treatment, both inducing hyperthermia when a proper alternate magnetic field is applied and releasing oxygen as radio-sensitizer for a subsequent radiotherapy session.