Rapid ex vivo imaging of PAIII prostate to bone tumor with SWIFT-MRI

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PURPOSE

Prostate cancer will claim the lives of approximately 27,000 men in the US alone in 2012 [1]. Of the men that succumb to the disease, studies have shown that up to 90% will have evidence of bone metastasis [2]. Prostate to bone metastases are hallmarked by areas of extensive osteogenesis and osteolysis. Common side effects include hypercalcemia, pain and pathological fractures that greatly impact the patient's quality of life. Despite our knowledge of the molecular mechanisms underlying the disease, little is known in terms of defining which patients will relapse with metastatic bone cancer [3]. Early detection of metastases can be advantageous in terms of treatment and long term survival. The emerging MRI method Sweep Imaging with Fourier Transformation or SWIFT can detect MR-signals with broad range of T_2 relaxation times, including extremely short T_2's [4]. SWIFT uses a swept RF excitation and simultaneous signal acquisition in a time-shared mode in the presence of field gradients. It has already shown very promising results in detection of mandibular invasion by squamous cell carcinoma [5] and in dental imaging [6]. The purpose of this study is to assess the feasibility of SWIFT to visualize prostate-to-bone tumor in *ex vivo* specimens derived from pre-clinical animal models as well as to compare SWIFT images with CT, traditional MRI and histological sections.

METHODS

Luciferases expressing PAIII prostate cancer cells were injected (10^5 in 10 μl) into the tibia of an anesthetized immunocompromized mouse while contralateral limbs received sham injections of saline. After four weeks the animals were euthanized and limbs fixed in 10% formalin. Experiments were performed in a 31-cm, 9.4-T magnet. RF transmission and reception were performed with a home built, single loop, 17 mm- diameter coil. The SWIFT sequence had excitation bandwidth of 100 kHz, and a flip angle of 14^0. The pulse was oversampled by a factor of 16 [7]. Data were collected in 256 gaps of 6 μs each, when radio-frequency transmitter was off. The repetition time TR, including 2.56 ms pulse length, was 3.16 ms. Data in 3D k-space consisted of 128,000 spokes for high resolution images. The terminus of the k-space vectors described the isotropically distributed points on a sphere located in up to 16 interleaved spirals [8]. The total acquisition time was equal to about 10 min. Besides regular SWIFT, additional SWIFT experiments were conducted, in which MR-signals from fat and portion of water with long T_2 were suppressed. The suppression was achieved by applying 8 ms, 90^0 of double banded Gaussian pulse (focused at water and fat resonances) after each 8^{th} SWIFT readout. According to Bloch simulations, the use of such pulse effectively saturates all signals with T_2's exceeding 400 μs [9, 10]. For presentation, the long T_2 suppressed images (short T_2 images) were smoothed by 3D median filtering. In addition, conventional CT, gradient-echo and spin-echo (not shown here) images were collected. Gradient-echo parameters were: 10^0 flip angle, 2.9 ms echo time, 8 ms repetition time with 256^3 resolution. To capture spin-echo images at different echo times, 2D Multiple Echo Multi Shot (MEMS) sequence was used**.** It had a repetition time of 2 sec, while echo time was varying from the 5 ms to 40 ms. In all MRI experiments the FOV was 15^3 mm^3. CT source voltage and current were 60kV and 200μA. Rotation angle was 210^0 with 420 projections. Binning 1 and high magnification were used with exposure time of 9sec and total scan time of 100min.

RESULTS and CONCLUSION

Representative SWIFT, CT and gross histology images for sham injected and PAIII prostate tumor bearing tibia are illustrated in figure 1. Resolution for SWIFT and CT images is 58 and 15 μm respectively. For sham tibia regular SWIFT shows relatively uniform signal from the medullary cavity and hypointense (dark) signal from the surrounding cortical bone. Cortical bone along with trabecular bone was observed on long T_2 saturated SWIFT images, which is a low contrast image by nature. Normal uniform marrow and trabecular bone patterns can be identified in histological sections and high resolution CT respectively. Overall, as expected, all sham tibia images are quite uniform. In contrast to the sham injected controls, the tumor bearing tibia displayed areas of cancer induced bone formation and resorption (Fig.1, B2). In tumor bearing limb, CT analysis identified irregular bone growth as opposed to the regular lattice-like trabecular bone pattern observed in sham tibia. In tissue sections, the prostate cancer is clearly visible as light pink area in the upper medullary cavity (B4). While seen as brighter region on spin echo with 30 ms echo time (not shown here), the long T_2 tumor signal is completely absent on long T_2 saturated SWIFT, where tumor appears as dark area and shows negative contrast with surrounding regions (B2). In addition, tumor induced bone formation, a characteristic commonly associated with prostate-to-bone metastases, was identified in the same image, and is in agreement with CT analysis (B5). These results demonstrate that SWIFT with saturated long T_2 has the capacity to identify both tumor and tumor induced bone formation in the same image.

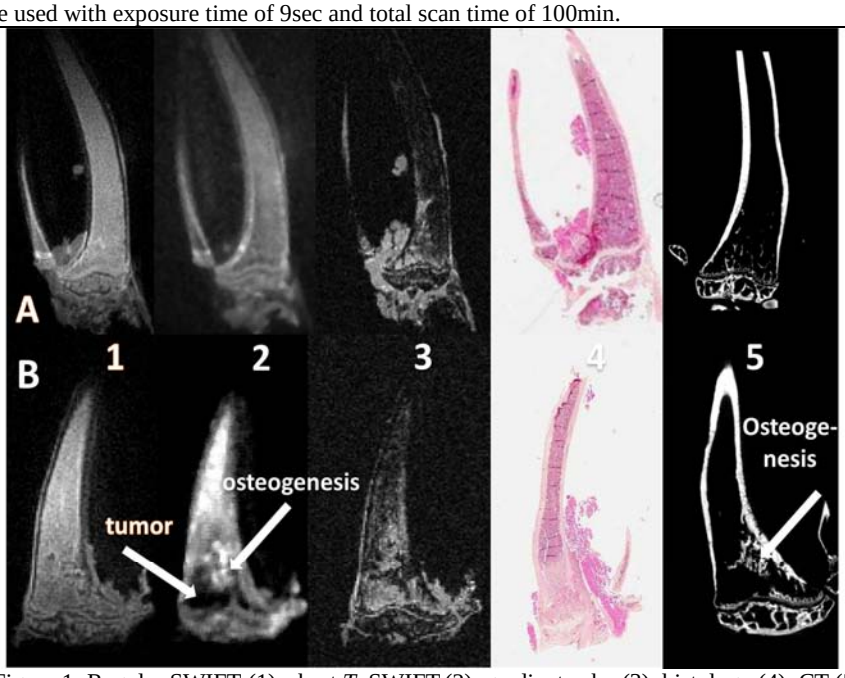

Figure 1: Regular SWIFT (1), short T_2 SWIFT (2), gradient echo (3), histology (4), CT (5) images of bone with sham (A) and tumor (B)

REFERENCES

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