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CONTROL ID: 2218021
TITLE: Spectroscopic Photoacoustic Molecular Imaging of Breast Cancer Using an Antibody-Dye Contrast Agent
PRESENTER: Katheryne Wilson
ABSTRACT BODY:
Abstract Body: Introduction: Spectroscopic photoacoustic (sPA) imaging allows for identification of individual optical absorbers within biological tissues, endogenously limited to hemoglobin, melanin, and lipids. Molecularly specific contrast agents are needed to investigate other tissue markers, but few agents are considered readily clinically translatable. Our objective was to explore the potentially clinically translatable combination of antibodies (Ab) and the FDA-approved near-infrared, fluorescent dye indocyanine green (ICG) for sPA imaging of CD276, a molecular marker differentially expressed in breast cancer[1], which may improve accuracy of ultrasound imaging for breast cancer detection.
Methods: Succinimidyl ester modified ICG was conjugated to monoclonal Ab specific to the CD276 marker. Ab-dye binding ratios were determined using spectrophotometric analysis and protein concentration was determined with a standard BCA assay. A transgenic mouse model for breast cancer development (FVB/N Tg(MMTV/PyMT634Mul) was used to assess the ability of sPA imaging to detect the accumulation of CD276-ICG contrast agent in breast cancer. Mice with invasive breast adenocarcinoma (10-12 weeks of age) were injected intravenously with 33 μg of CD276-ICG or control agents, including isotype Ab conjugated with ICG (Iso-ICG), ICG dye alone, or CD276-ICG in tumor negative mice. Fluorescence, multi-wavelength (680-950 nm, 10 nm increments) sPA, and B-mode ultrasound imaging were performed before and 24h, 48h, and 72h after i.v. administration using the VisualSonics LAZR and the Xenogen IVIS Spectrum. Anatomical B-mode images were used to guide ROI selection for sPA data analysis. Using an in-house sPA data analysis algorithm, the average molecular CD276 signal in the tumor ROI was determined by monitoring absorbance shifts of ICG. CD276-ICG uptake and clearance were monitored with fluorescence imaging. Immunohistochemical (IHC) staining was used to quantify CD276 expression in breast cancer and normal mammary gland tissue.
Results: In total, 80 tumors were imaged over the five day period with another 110 monitored with various control agents (Iso-ICG (n= 30), CD276-ICG in normal mammary glands (n = 60), and ICG only (n=20). Tumors showed a 3.15±0.42 fold increase in molecular CD276 signal compared to pre-injection values with sPA (range 0.30–20.0 fold increase, $p<0.001$) and a 1.37±0.15 fold increase in CD276 signal with fluorescence imaging (range 0.75–2.02 fold increase, $p<0.001$). Control agent values showed no significant increase in signal compared to background values. Murine breast cancer tissue, both epithelial and endothelial cells, stained positive for CD276, while normal tissue did not express CD276.
Conclusions: Spectroscopic photoacoustic imaging is able to detect clinically translatable antibody-dye contrast agents in a transgenic mouse model of breast cancer. CD276-targeted molecular sPA signals were detected as early as 24 hours and for at least 96 hours after injection. Molecular sPA imaging may become a complementary parameter to ultrasound imaging for more accurate earlier detection of breast cancer.
1. Seaman S., et. al. *Cancer Cell*. 2007;11(6):539-554
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CONTROL ID: 2222131

TITLE: Computational MR Model for Characterizing Atherosclerotic Plaques Morphology and Composition

PRESENTER: Michael Dada

ABSTRACT BODY:

Abstract Body: Introduction

Most studies of atherosclerotic plaques have focused on the assessment of degree of stenosis [1]. However, an anomaly has been noticed which suggests that plaque size is not always a determining factor in patient symptomatology and that other plaque features may play a significant role in plaque pathogenicity [1].
Recent clinical and patho-anatomic observations indicate that plaque composition and biology are more significant determinant than plaque size in the development of thrombus-mediated acute coronary syndromes [1]. Thus clinical risk may correlate more closely with plaque morphology and surface features than with size [1]. This possibility emphasizes the importance of developing non-invasive imaging methods for characterizing plaque morphology and composition in addition to determining lumen area and wall thickness.

Methods

For this study, we shall consider spin dynamics of arterial blood and surrounding tissues based on the time-independent Bloch NMR flow Eqn [2]. Within a rotating frame, Larmor condition holds (Eqn (1)) and provided that the bulk protons are moving at a variable velocity v(x), the NMR Bloch flow eqns is given[2] in Eqn (2). If the RF field $B_1(x)$ is applied such that M_y is sampled at max. magnitude, $M_0 \approx 0$. Eqn (2) therefore becomes Eqn (3). If the assumptions in Eqn (4) holds, we have a Bessel diff. Eqn (5). For M_y signal which is measurable at all points x and if C_1 is the amplification constant, solution to Eqn (5) is given in Eqn (6).

Results

From recent experimental studies [3, 4], arterial blood and plaque components have relaxation constants at 9.4T as presented in Table 1. From the results expressed in Eqn (6), we have developed a Python computer program. The resulting GUI is presented as Fig. 1. Figs. 2 give the M_y map of arterial blood and plague components at 9.4T.

Discussions

We have demonstrated possibility of performing computational MRI to spatially localize different components of atherosclerotic plaques in carotid arteries ex vivo. Using Table 1, we were able to obtain unique images for different plaque components and arterial blood. What is interesting in this work is that few NMR data are required for plaque imaging and the model is capable of interpolating for data points which are impossible because of NMR hardware restrictions.

Conclusion

The computer program may also prove to be very useful in monitoring the effects drugs for treatment of atherosclerotic lesions and in identifying, localizing and quantifying plaque components in 3D. It provides a time-friendly simulation platform for imaging, monitoring drug administration/testing and repetitive running of NMR data.

Acknowledgement

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References

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