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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: 2222139

TITLE: Computational Model for Comparative Analysis of MRI Contrast Agents

PRESENTER: Michael Dada

ABSTRACT BODY:

Abstract Body: Introduction

The efficacy of MRI contrast agents (CAs) is not only determined by their pharmacokinetic properties but also by their magnetic properties as given by their T_1-and T_2-relaxivities [1,2]. It is very important to conduct comparative investigation on a large number of MRI CAs because their properties are dependent on different physiological environments (PEs) & binding to macromolecules in the blood [2]. Hence, different CAs are designed for different imaging objectives. However, the individual linearities of relaxation rates vs concentration is difficult to quantify using the experimental measurements in a wider concentration range due to the large amount of samples investigated at several magnetic field strengths and in different solvents [2]. Hence, we have developed a model and computer program for comparative analysis of NMR profiles of CAs in different PEs.

Methods

We consider spin dynamics of CAs & surrounding tissues based on Bloch NMR flow Eqn (BNFE) [3, 4]. Within a rotating frame, Larmor condition exists such according to Eqn (1). In the instance at which the molecules of the CAs are in motion at a variable velocity v(x) and the relaxation times of the solvent without the CA is T_{i0} (i = 1, 2) [2], the BNFE is [3, 4] given as Eqn (2). Note that C is the concentration of the CA while r_1 and r_2 are the relaxivities. Assuming that fluid velocity & the applied field have the forms expressed in Eqn (3), we then have Eqn (4). Because of the difficulties in obtaining analytical solution to Eqn (4), we employed Mathematica 9 software from where we got Eqn (5).

Results

A Mathematica code is also developed based on Eqn (5). Using relaxometric parameters of GADOVIST, MULTIHANCE & Gadomer in Plasma (T_{10} = 1.4493s, T_{20} = 0.3846s) & blood (T_{10} = 1.1111s, T_{20} = 0.2174s) at 37^0 C, B_0 = 1.5T [2]; setting C_1 = 2000, C_2 = 100 & M_0 = 100A/m, we have Figs. 1 & 2.

Discussions and Conclusion

It is worthy of note that for each of the CAs considered, the program showed unique M_y profiles & the model demonstrate the ease at which M_y of different CAs may be compared within different tissues/solvents. All that we require are the relaxometric & NMR parameters (such as gradient magnitude & pulse duration) of the CAs. In fact, large number of CAs may be compared in a very short time. In conclusion, we have developed a program which could make life easier for NMR scientists in terms of managing CAs for different physiological interests and they can now run as many simulations as possible before injecting the CAs into living systems.

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