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Contact: Aloma D'Souza
INSTITUTION: Stanford University E-Mail: aloma.dsouza@stanford.edu

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01) Low-Frequency Ultrasound Amplifies the Release of Multiple Tumor Biomarkers in Living Subjects

A L D'Souza, MS, PHD; J Tseng, MD; J Rosenberg, PhD; K R Butts-Pauly, PhD; S S Gambhir, MD, PhD; G M Glazer, MD, Stanford, CA (glazer@stanford.edu)

PURPOSE

Low frequency ultrasound is known to compromise the permeability of cell membranes; we hypothesize and prove that this bioeffect of ultrasound can be used to release multiple biomarkers into the extracellular milieu. The release of biomarkers into circulation could lead to the earlier detection of cancer and identification of unknown incidental lesions.

METHOD AND MATERIALS

Cancer cell lines (colon-LS174T; prostate-LNCaP) that produce biomarkers (CEA, CA19-9; PSA) were exposed to 1 MHz ultrasound in culture using various intensities and time. Subcutaneous tumors (>0.3cm3) of LS174T in mice (n=7 per group; n=28 total) were also sonicated directly over the tumors. Controls were sonicated on non-tumor bearing regions. The biomarkers were detected in culture media or murine blood samples, pre and post-ultrasound application, using an enzyme-linked immunosorbant assay.

RESULTS

Application of 1 MHz ultrasound pulses to cultured LS174T cells at various intensities was shown to amplify the CEA released into the media. Treatment of the cells (n=4) at a low intensity of 0.3 W/cm2 at 1 MHz and 10% duty cycle, showed an increase in release of both biomarkers CEA and CA 19-9 with time (0, 10, 30 min; $p<0.05$). The prostate cancer cell line LNCaP also showed substantial increases of PSA released in culture media both with an increase in intensity as well as with time. Subcutaneous tumors of LS174T showed a significant increase in CEA levels released post sonication at 2 W/cm2; 50 % duty cycle for 6 min ($p<0.03$), compared to the controls.

CONCLUSION

Increases in biomarker release were observed when ultrasound was directly applied to cells or tumors in living mice. We have demonstrated a novel method to amplify and localize multiple biomarkers using ultrasound. This provides a new way for Radiology and medical imaging to become involved in personalized medicine by using image-guided ultrasound to perturb lesions and release biomarkers from them. This has implications in both diagnosis and monitoring of therapy and points towards the ultimate use of focused ultrasound to amplify biomarker release in humans.

CLINICAL RELEVANCE/APPLICATION

We have developed a new method, using ultrasound to amplify and localize biomarkers signals, which brings radiology into the realm of personalized medicine.

FIGURE (OPTIONAL)

**** no data entered ****

Disclosures:

Nothing to disclose:	Aloma D'Souza
Nothing to disclose:	Jeffrey Tseng
Nothing to disclose:	Jarrett Rosenberg
Nothing to disclose:	Kim Butts-Pauly
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