World Molecular Imaging Conference 2010 – 2010 Winner in category

Localization and Characterization of Tumors by Ultrasound-Induced Release of Multiple Biomarkers

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Ultrasound at low frequencies has been used for drug delivery due to its effect of permeabilization of cellular membranes. We hypothesize and prove that this bioeffect of ultrasound also causes the extracellular release of multiple biomarkers from cells in culture and in living mice. The increased release of biomarkers could lead to the identification of incidental lesions and earlier detection of cancer and other disease. The ability to focus ultrasound and confine it to a defined area, allows for localization of the source of the biomarker release.

Materials/Methods: Cancer cell lines (colon-LS174T; prostate-LNCaP) that produce biomarkers (CEA, CA19-9; PSA) were exposed to varying intensities and time of low frequency (1 MHz) ultrasound in culture and in subcutaneous tumors of the cells in living mice. The released biomarkers in the cell culture supernatants or serum of the mice were detected using an enzyme-linked immunosorbant assay.

Results: LS174T cells treated with 1 MHz ultrasound at a low intensity of 0.3 W/cm^2 was shown to release CEA and CA19-9 with an increase in time (0, 10, 30 min; $p<0.05$). These cells were also shown to increase the release of the biomarkers in serum of mice when ultrasound at 2 W/cm^2 was applied to subcutaneous tumors (CEA $p<0.04$; CA19-9 $p<0.002$). Controls treated with ultrasound on non-tumor sites of tumor-bearing mice did not show any increase in the release of biomarkers. The prostate cancer cell line, LNCaP, in culture also showed a substantial increase in the release of PSA with ultrasound treatments.

Conclusions: Low frequency ultrasound releases multiple biomarkers only when directly applied to cells or tumors. This allows for the spatial localization of tumors expressing the biomarkers as well as characterization of unknown tumor mass due to the biomarker amplification. This has further implications for monitoring the therapy of lesions. The clinical applications for the use of MR image-guided focused ultrasound for this method of biomarker localization and release would be straightforward and bring together the fields of imaging and *in vitro* diagnostics.

Category choice:
Ultrasonic Imaging and drug delivery

Keywords: (choice of 3)
Biomarker, ultrasound, membrane, permeability