Noninvasive MR imaging of blood vessel growth in tumors using nanosized contrast agents

July 23 2010

Formation of new blood vessels, also known as angiogenesis, is crucial for sustained tumor growth and cancer metastasis. Recently, clinically available therapies to suppress the growth of these vessels have been available to improve patient survival in some cancer types. Accurate detection and quantification of blood vessel growth using nonsurgical methods would greatly complement current therapies and allow physicians to quickly assess treatment regimens and adjust them as necessary.

In the work published in the August issue of Experimental Biology and Medicine, Kessinger and coworkers have incorporated nanotechnology, material science, and the clinical imaging modality MRI, to create a nanosized probe capable of noninvasively visualizing and quantifying the blood vessel growth in tumors in a preclinical model. The work was carried out by Chase Kessinger, as part of his PhD thesis in cancer molecular imaging, working together with Jinming Gao and other colleagues, at the University of Texas Southwestern Medical Center at Dallas.

Dr. Gao stated "Imaging tumor angiogenesis is important in early detection, tumor stratification and post-therapy assessment of antiangiogenic drugs. Current clinical modality for angiogenesis imaging utilizes dynamic contrast enhancement MRI by small molecular contrast agents. The method is based on the measurement of permeability of the

contrast probes in well-established solid tumors and is not very specific to detect the early on-set of vessel formation. The dual functional nanoprobes aim to image angiogenesis-specific tumor markers that are overly expressed in the tumor vasculature during the early phase of angiogenesis."

Together, the research team relied on nanotechnology and established super paramagnetic micellar nanoprobes (50-70 nm in diameter) with greatly improved MRI sensitivity over conventional small molecular agents. The nanoprobe surface was functionalized with integrins that are a cyclic peptide that can specifically bind to overexpressed on the tumor endothelial cells. The nanoprobes also had a fluorescent moiety used for the validation of targeted delivery to the tumor endothelial cells. Studies in cancer cells validated the increased uptake of nanoprobes compared to non-targeted-nanoparticles. In collaboration with Dr. Masaya Takahashi and coworkers in the Advanced Imaging Research Center at UT Southwestern Medical Center, the research team employed a 3D high resolution acquisition method to visualize the accumulation of the micelle nanoprobes in tumors.

Dr. Gao said "Conventional image analysis of angiogenesis relies on the evaluation of 'hot spot' densities in 2D images. The 3D high resolution method allowed for the connection of the isolated 'hot spots' in 2D slices into 3D network structures, which greatly improves the accuracy of vessel identification and quantification."

In preclinical animal tumor models, MR imaging of the targeted contrast probes yielded vascularized network structures in 3D tumor images. The enhanced visualization allowed for a more accurate quantification of tumor angiogenesis. The results showed significant increase of contrast specificity of angiogenic vessels by the targeted nanoprobes over non-targeted micelles. These targeted nanoprobes may provide a useful contrast probe design for the clinical diagnosis of tumor angiogenesis.

Steven R. Goodman, Editor-in-Chief of Experimental Biology and Medicine, said "Kessinger et al working at the interface of nanotechnology, material science, and the clinical imaging modality MRI have created a nanosized probe capable of noninvasively visualizing and quantifying the blood vessel growth in tumors in a preclinical model. This should be an important tool for clinical observation of tumor angiogenesis".

Provided by Society for Experimental Biology and Medicine