MRA Microvascular Mapping of Lungs for Early Diagnosis of Cancer in Primary and Second-Hand Smokers

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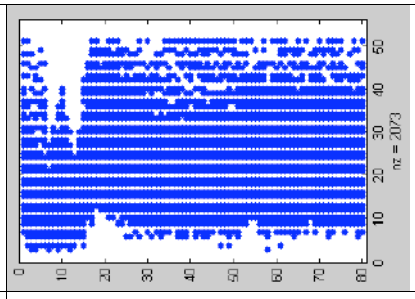
Background: Lung cancers are commonly diagnosed by transthoracic needle aspiration biopsy, which carries the risk of major complications including pneumothorax and hemoptysis. However, sensitivity is not as high, as 30-40% of patients with initial negative cytology are later found to have a malignant lesion. In the Early Lung Cancer Action Project (ELCAP) (Henschke CI,1999), nodules were detected in 21% of subjects without lung cancer. In addition, about one sixth of all lung cancers found at autopsy had not been clinically recognized before death (Chan CK, 1989).

Methods: Thirteen patients with pulmonary nodules were invited to participate in a MRA study of microvascular development, majority smokers (n=6) or secondhand smokers (n=4). Patients were imaged in coronal view centered on region of interest using a 1.5T GE Excite dual gradient system. Images were obtained every heartbeat for 80 consecutive frames using FGRET, matrix (256x256), during bolus transit of 20cc MAGNEVIST® (gadopentetate dimeglumine, Berlex) injected at 4cc per second. Automated motion tracking was implemented to correct for minor respiratory shifts. Images were analyzed by converting sequential frames to 80-tuple vectors for each pixel which were analyzed for fit to vessel groups by two separate models, one for large vessels and one for microvessels, for arrival and departure of a contrast reagent in a vessel.

From our MRI data, for each lesion, four different regions of interest were characterized: (1) each nodule, (2) the area around each nodule excluding the nodule (penumbra), (3) an identical size region the same distance from the pleura in the same lung but more than 5 cm from any nodule, and (4) the location corresponding to a nodule but in the opposite lung. To analyze the fractal pattern, we used the box counting method with five iterations, measuring fractal dimension as 1-slope of the natural logarithm of box size versus the natural logarithm of box size multiplied by total number of positive boxes.

Results:

(a) Cancer penumbra fractal dimension 1.71.
(b) Opposite lung fractal dimension 1.66
Overall: 1.73 v. 1.79, p<0.003



a b

Four patterns of vascular enhancement were observed: (1) late arterial phase progressive microvascular enhancement (PME), (2) oscillatory arterial enhancement (OAE), (3) early arterial phase wash in and wash out (EAE), and (4) no evident enhancement. Pattern 1 corresponded to cancer, and 2 to inflammatory lesions, while 3 and 4 in the absence of 1 or 2 corresponded to benign findings. Mean time-fractal dimension of cancer penumbra was 1.727±0.007 vs. control 1.791±0.009, $p < 0.0003$, whereas benign nodules had no significant difference. Inflammatory nodules exhibit an oscillation suggestive of shunting.

Conclusions: Modeling of time series images during bolus transit of contrast can extract maps of the microvascular contribution yielding fractal measurements that appear to identify early cancers.