Systemic prostate specific antigen (PSA) is a measure of vascular permeability and not malignancy: A Prostate Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) Study.

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Introduction:

Prostate cancer is a major cause of morbidity and mortality in American men. Given the importance of early detection, PSA levels have been used as a measure of the likelihood of malignancy and extracapsular spread of the disease. The major focus has been on correlating PSA with malignancy and less on the relationship between PSA and vascular changes occurring within the prostate[1-3]. It is our hypothesis that systemic PSA levels correlate with vascular permeability changes and not necessarily with malignancy. Dynamic dynamic contrast enhanced MRI (DCE-MRI) can well characterize the extent and variation in permeability of prostate vasculature.

Materials and Methods:

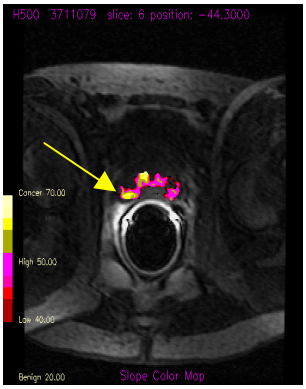
Thirty two patients enrolled under the Comprehensive Prostate Protocol, National Institutes of Health (July 2002-current) were examined using endorectal dynamic contrast enhanced MRI (DCE-MRI). Serum PSA levels were determined prior to the imaging study. Biopsy was performed for diagnosic evaluation. The DCE-MRI exam consisted of the following 3DFSPGR sequence, TE <1ms, TR 4ms, Flip 30^{o}, BW 62 kHz, FOV 24-26cm, slice thickness 5-7 mm, 256x128 matrix, 0.5 NEX, injection rate: 0.1mmol/kg at 3cc/sec, (total time, ~ 4 minutes). The images from DCE-MRI were evaluated using an in-house image processing program, (IDL). The slope of the initial contrast enhancement curve was measured and a "volume of high permeability" (HPV) was determined for each prostate gland as an indication of total vascular permeable area. The patients were grouped into three categories as defined by their PSA levels: Group 1 had low serum PSA levels of < 4.0 ng/ml, Group 2 had moderate serum PSA levels ranging from 4.0-20.0 ng/ml, and Group 3 had high serum PSA levels that were > 20ng/ml.

Results:

The average serum PSA and HPV value for the low, moderate and high PSA groups was: Group 1(N=4): PSA 1.25 $\pm$ 1.05 ng/ml and HPV 3.5 $\pm$ 4.4; Group 2 (N=22): PSA 7.0 $\pm$ 2.7 ng/ml and VHS 12.8 $\pm$ 15; Group 3 (N=6): PSA 23.0 $\pm$ 13.0 ng/ml and HPV 19.35 $\pm$ 8.5. There was a significant difference between both PSA (P= 0.009) and HPV (P=0.005) values between Group 1 and Group 3 (student t-test) indicating patients with high vascular permeability have high serum PSA levels and patients with low HPV have low PSA levels. In further support of our hypothesis, two patients in the low PSA group had cancer, while two patients in the high PSA group were diagnosed with prostatitis with no presence of malignancy.

Conclusion:

This initial study indicates that in addition to the production of PSA by prostate cells, vascular permeability also plays an important role in serum PSA levels in both cancerous and none malignant prostate tissue. Other serum markers for disease such as CEA may have similar correlation with vascular changes and angiogenesis.



References:

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Figure 1. Color map of contrast uptake on DCE-MRI of 63 yo man with prostate adenocarcinoma, PSA = 6.9, HPV=12.4, arrow shows prostate region with rapid uptake of contrast.