DCE-MRI Demonstrates Antivascular Properties of Sorafenib in Metastatic Hormone-Resistant Prostate Cancer

M. A. Rosen[1], G. Adluru[1], R. Amaravadi[2], Y. Xue[1], Y. Jiangsheng[1], H-K. Song[1], N. Haas[2], and P. O'Dwyer[2]
[1]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Medicine, University of Pennsylvania, Philadelphia, PA, United States

Background: Dynamic contrast enhanced MRI (DCE-MRI) can be used to monitor effects of anti-vascular therapies in vivo[1]. Volumetric DCE-MRI with radial acquisition can improve exam implementation by allowing for large volume coverage while maintaining the ability to rapidly track contrast kinetics through K-space weighted image contrast (KWIC) post-processing[2,3]. We obtained 32-slice whole-pelvis imaging in a cohort of hormone-resistant metastatic prostate cancer (HR-mPC) patients receiving combination therapy with sorafenib and taxotere. Therapeutic monitoring of response in this regimen is problematic as sorafenib has been shown to cause paradoxic rises in serum PSA[4], the tumor response marker measured in prostate cancer therapy trials.

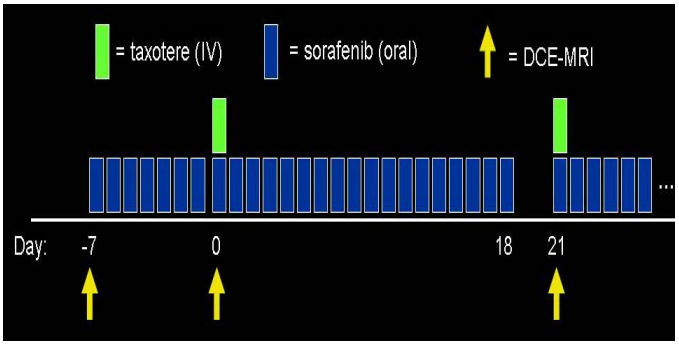

Figure 1: Trial schema. Note sorafenib "holiday" prior to DCE-MRI #3.

Methods: IRB approval for study was obtained. The schema for the trial is shown in Figure 1. Thirteen patients with HR-mPC were treated with sorafenib and taxotere, including a one-week (day -7 to day 0) run-in phase with twice daily oral sorafenib alone, followed by 21 day cycles of day 1 IV taxotere with ongoing twice daily oral sorafenib for days 1-18. DCE-MRI was performed on day -7, day 0, and day 21. Radial DCE-MRI was performed in the axial plane with FOV=380mm, matrix=192x192, TR=3.17ms, TE=1.45ms, slices=32, slice thickness=6.25mm, with 21-view sliding window KWIC to achieve 1.7s temporal resolution. Osseous and soft tissue tumors were manually segmented on the central 28 slices from the DCE-MRI images. AUC60 was computed from gadolinium-time curves using S(t)/S(0) signal ratios and assumed tumor T1=850ms.

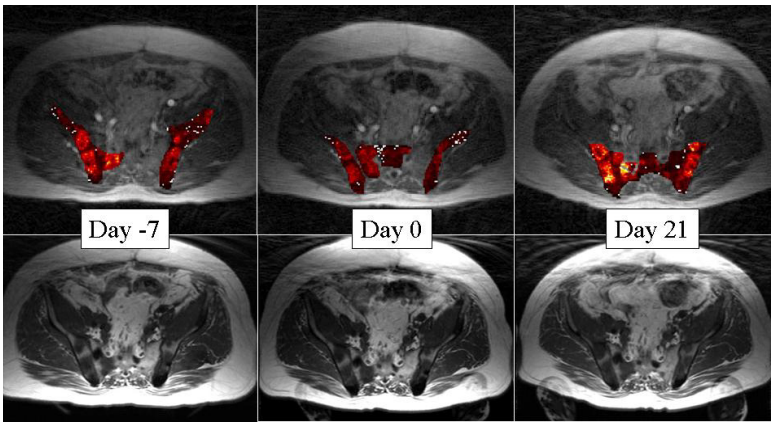

Figure 2: AUC60 color maps (top) and T1 SE images (bottom) for a representative patient at day -7, day 0, and day 21. Note day 21 tumor AUC60 rebounds to values approaching baseline, reversing the decline in AUC60 noted on day 0.

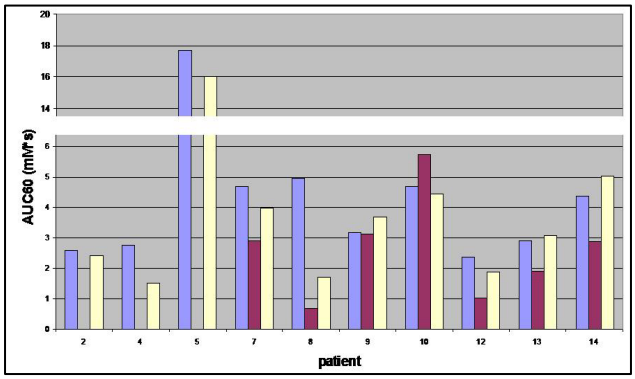

Figure 3: Median pixel AUC60 values for patients with osseous metastases. Day -7 (blue), day 0 (red), and day 21 (yellow).

Results: Eleven patients received DCE-MRI at day -7 and at day 21. Seven of these patients also received DCE-MRI at day 0. For these seven patients, median pixel AUC60 for osseous metastases at day 0 declined by an average of 33% from day -7 values, but only declined by 10% between day -7 and day 21, with several patients showing AUC60 "rebound" at day 21 (Figures 2 & 3). Results were similar for soft tissue metastases (ΔAUC60 = -37% between day -7 and day 0; ΔAUC60 = -17% between day -7 and day 21. Lack of change of AUC60 between day -7 and day 21 AUC60 was seen across the majority of patients.

Conclusion: Volumetric DCE-MRI can be used to demonstrate vascular response of metastatic prostate cancer to sorafenib. DCE-MRI measures of tumor vascularity three days after suspension of sorafenib at end cycle one shows return toward baseline values. Further study is required to determine how rapidly reversible the anti-angiogenic effects of sorafenib are upon drug cessation.

References:

1. Padhani AR. J Magn Reson Imaging. 2002 (4):407-22. 2. Song HK et al. Magn Reson Med. 2004 (4):815-24.
3. Lin W et al. Magn Reson Med. 2008 (5):1135-46. 4 Chi KN et al. Ann Oncol. 2008 (4):746-51.