Dynamic Contrast-Enhanced MRI as a Predictor of Residual Tumor after Photodynamic Therapy with TOOKAD (WST09) for Locally Recurrent Prostate Carcinoma after Radiation Therapy

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Introduction: Patients with local recurrence of prostate cancer after external beam radiation therapy may benefit from local ablative therapy. WST09 (TOOKAD, Negma-Lerads, France) is a photodynamic agent that exhibits anti-vascular activity when activated by laser light. Dynamic contrast enhanced MRI (DCE-MRI) has been show to delineate tissue necrosis after photodynamic therapy with WST09 (TOOKAD-PDT) (1,2). DCE-MRI can help delineate cancer in the peripheral zone of the prostate (3). If these methods were combined, it may be possible to predict whether tumor had been completely treated after partial prostate ablation.

Purpose: The purpose of this study was to determine if DCE-MRI could predict the presence or absence of residual tumor after TOOKAD-PDT.

Methods: 17 men with locally recurrent prostate cancer after radiation therapy were treated with TOOKAD-PDT as part of a Phase I/II trial. DCE-MRI was performed pre-therapy and 7 days post-therapy. Images were obtained with a 1.5T MRI system (Excite HD, GEMS, Milwaukee, WI) using an 8 element torso phased array surface coil and a 3D fast spoiled gradient echo sequence with TR 8.7ms, TE 4.2ms, matrix 256x160, 3/0mm, temporal resolution 95s and fat saturation. Nine phases were acquired with 2 baseline phases obtained prior to contrast injection at the start of the third phase (4ml/sec, 0.1mmol/kg, Gd-DTPA). Focal regions showing enhancement equal to or great than the transition zone on the first post contrast phase of the pre-treatment MRI were considered cancerous. Regions showing no enhancement on the last post enhancement phase of the 7 day MRI were considered necrotic. If the prostate showed a region of cancer on baseline DCE-MRI and the corresponding region did not show complete necrosis on the 7 day post therapy DCE-MRI this was considered a incomplete treatment (Fig 1 & 2). Systematic sextant biopsies were performed at 6 months post therapy and used as a reference standard for the presence or absence of residual tumor.

Results: 10/17 men had residual tumor at 6 months. On a patient by patient basis DCE-MRI was able to predict residual tumor after TOOKAD-PDT with sensitivity 10/10 (100%), specificity 5/7 (71%), PPV 10/12 (83%), NPV 5/5 (100). For each prostate half the sensitivity was 11/11 (100%), specificity 18/23 (78%), PPV 11/16 (69%), NPV 18/18 (100%).

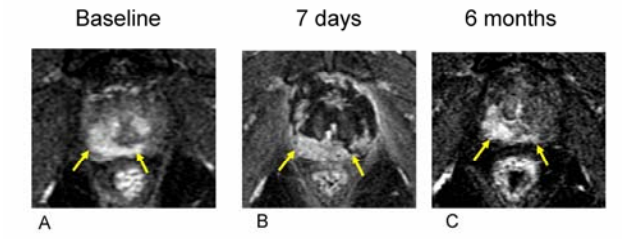

Fig 1 Incomplete treatment
A) Pre-treatment DCE-MRI early post contrast enhanced image shows a large region of tumor in the right peripheral zone extending to the right. B) Post therapy delayed image shows necrosis (dark region) that spares the region of tumor seen at baseline (yellow arrows). C) At 6 months early post contrast enhanced image shows residual tumor confirmed by biopsy

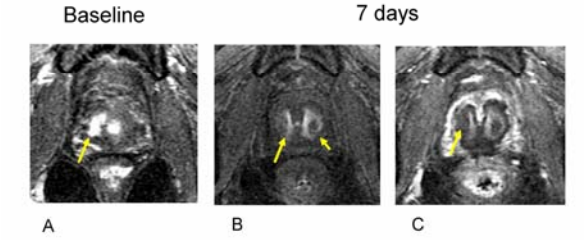

Fig 1 Complete treatment
A) Pre-treatment DCE-MRI early post contrast enhanced image shows tumor in the right anterolateral peripheral zone. B) Post therapy pre-contrast image shows some haemorrhage. C) Discounting the haemorrhage, delayed image shows necrosis (yellow arrows) that encompasses the region of tumor seen pre-treatment. No tumor was found at 6 month biopsy.

Discussion: We have demonstrated that baseline and post TOOKAD-PDT DCE-MRI can be combined to determine if the tumor has been completely treated. The findings suggest that DCE-MRI can play an important role in not only delineating treatment response in this population but also help guide therapy and determine whether re-treatment is necessary without the need for repeat biopsy.

Conclusion: The results of this Phase I-II study indicate that DCE-MRI is an accurate method for predicting the presence of residual tumor after TOOKAD-PDT.

References

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