Apparent Diffusion Coefficient Changes in Areas of Prostatic Necrosis Following Photodynamic Therapy in Patients with Local Recurrence of Prostate Cancer

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Introduction: Patients with locally recurrent prostate cancer after radiation therapy can benefit from therapy designed to eradicate tumor. WST09 (TOOKAD®, Negma-Lerads, France) is a novel intravascular photosensitizer. When injected intravenously and activated locally by 763 nm laser light it enhances rapid coagulation of blood vessels. This is followed by blood stasis producing necrosis that can be tumor selective. Diffusion weighted imaging (DWI) might be a good way to monitor therapeutic effect as one would expect necrotic regions to show an increase in apparent diffusion coefficients (ADC) because of increased free water.

Purpose: To determine the changes in ADC after WST09 photodynamic therapy (TOOKAD-PDT) in areas of prostatitic necrosis in patients with locally recurrent prostate cancer following radiation therapy.

Methods: Twenty-two patients received escalated WST09 and light doses as part of a PhaseI/II trial. Two optical fibers with cylindrical diffusing tips were connected to a laser, placed transperineally into each lobe of the prostate under ultrasound guidance and localized for registration with the MRI. WST09 was then injected intravenously and the prostate was illuminated. MRI was performed prior to therapy and seven days post therapy using a 1.5T system (Twinspeed Excite, GEMS, USA) and a 4-element torso phased-array coil. T2 weighted RARE (TR/TE 3800/98ms, ETL 10, FOV 20cm, 4/1mm, 256x192) and DWI were performed in 14/22 patients (EPI, BVal 600 s/mm^2, TR/TE 4000/105ms, FOV 20-30cm, 9/1mm, 16NEX, 128x128). Areas of necrosis were defined using axial T1 weighted fat saturated post gadolinium enhanced imaging performed 5 minutes post injection of 0.1mmol/kg of gadodiamide (TR/TE 650/20ms, FOV 20cm, 4/1mm, 256x192). Unenhanced areas were considered necrotic. This method of assessing necrosis was previously validated in a dog model (unpublished data). ADC maps were generated using Functool 2 (Adv.Windows Workstation v4.0, GEMS, USA). For each prostate half ADC was determined from the ADC map by drawing a 1cm diameter region of interest surrounding the fibre location on the pre and post TOOKAD-PDT ADC maps. ΔADC was defined as $ADC_{post\text{-}therapy} - ADC_{pre\text{-}therapy}$.

Results: Necrosis was present in 10/28 prostate halves. All necrotic areas showed a negative ΔADC with mean $ADC_{post\text{-}therapy}$ significantly lower than $ADC_{pre\text{-}therapy}$ ($p<0.005$). For areas of necrosis mean ΔADC was significantly different from zero ($p<0.005$) and significantly lower than mean ΔADC in prostate halves without necrosis ($p<0.0005$) (Fig 1). Mean ΔADC in non-necrotic prostate was not significantly different from zero ($p=0.1$) with a trend towards a positive ΔADC. Although relatively dark areas were seen in areas of necrosis on the post-therapy ADC maps, areas of necrosis were not as well delineated as on the post-gadolinium enhanced T1 weighted images (Fig 2). Necrosis was not well seen on conventional T2 weighted images.

Conclusion: ADC values drop in areas of prostatic necrosis 7 days post TOOKAD-PDT. TOOKAD-PDT is known to produce hemorrhagic and coagulative necrosis as opposed to liquefactive necrosis. One might expect less free water in coagulative necrosis and this may explain why there is a drop in ADC as opposed to the increase typically seen in necrotic tissue.

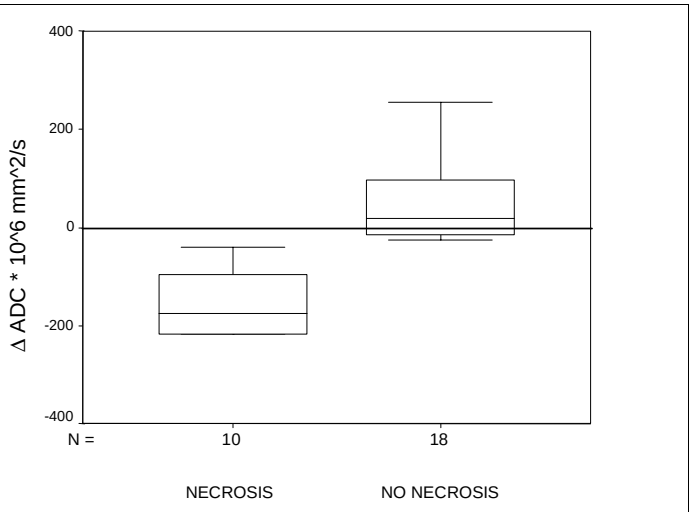

Fig 1. ΔADC in Regions of NECROSIS and NO NECROSIS
Regions of necrosis show significantly more ADC drop after therapy compared to non-necrotic areas

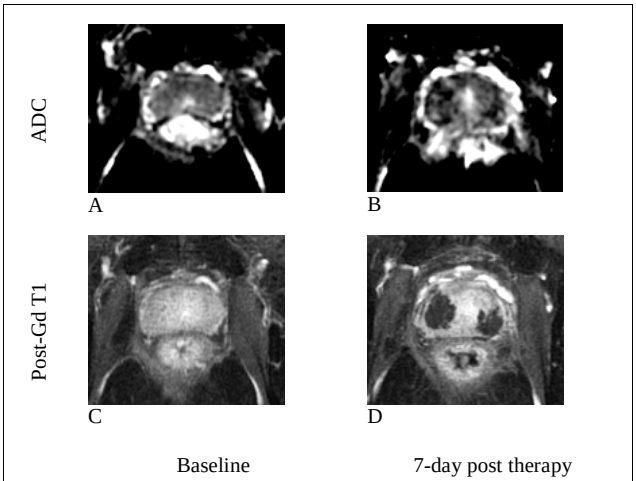

Fig 2. ADC Maps Pre-Therapy & 7 Days Post Therapy
Areas of necrosis are indicated by dark regions in D. Note dark areas (low ADC) in areas of necrosis (B) compared to baseline (A). Areas of necrosis are much better delineated on post-Gd T1 images (D)