High resolution dosimetry in monoenergetic proton beam therapy on a normoxic polymer gel: the importance of high spatial resolution for reduced Bragg-Peak-quenching.

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Abstract. Proton ion beam therapy demands for high resolution dosimetry due to the high dose gradients present in lateral confinement and final Bragg-peak. In polymer gels the reduction of the linear dose response in the area of the Bragg-peak is reported (Bragg-peak quenching), which is assumed to be mainly due to the high linear energy transfer (LET). We here investigate the impact of the spatial resolution in T2-mapping for accurate Magnetic Resonance Imaging (MRI)-based polymer gel dosimetry in the Bragg-peak for monoenergetic ion beams. We implemented MR-protocols for T2-mapping at microscopic resolution on a High-Field 7T human MR-scanner using an insert gradient system and sensitive rf-coils. The best results are obtained for an optimized polymer gel based on THPC with an optimized MR-protocol for reduced measurement time and sufficient SNR at 0,547 mm pixel size. The dose in the fine Bragg-peak could be measured correctly for a monoenergetic proton beam as confirmed by Monte Carlo dose simulations. Such high spatial resolutions at minimum are necessary for an accurate measurement of the dose in the sharp Bragg-peak for monoenergetic ion beams. We demonstrate that at higher pixel size the dose levels may be underestimated due to spatial averaging in MRI-based polymer gel dosimetry.

1. Introduction
Hadron beam irradiation concepts aim on the fine dose placement at the tumour site leaving nearby healthy tissue at minimum dose. The main advantages of ion beams are represented by the possibility for precise lateral confinement and dose enhancement at penetration depth (“Bragg-peak”, see fig. 1). Ionization-chambers represent the standard for the verification of treatment planning systems for proton therapy [1]. Also 2D-arrays of pin-point ionization chambers, film dosimetry and polymer gel dosimetry are used for the 3D-dosimetry of complex fields [2-4]. With regard to 3D-dose verification for patient treatment high spatial resolution is possible but critical [5-7]. The MR-Parameter T2 has shown to be most sensitive to the polymerization process in polymer gels subsequent to irradiation [8-10]. However the application of MR-based polymer gel dosimetry (MRPD) on ion beams is restricted by mainly three physical principles: 1.) the spatial resolution in T2-MRI [5] 2.) the signal-to-noise ratio (SNR) in MRI and consequently dose 3.) edge enhancement effects due to monomer diffusion [11] and 4.) a quenching of the dose response in the Bragg-peak-regime due to high LET [12].
In this contribution we investigate: 1.) the point spread function (PSF) in T2-micro-imaging on a human high-field (7T) MR-scanner equipped with a micro-imaging insert, 2.) the achievable T2-noise within reasonable MR-scanning time (11min), 3.) the influence and importance of the spatial resolution in MRI on the detected dose level in the Bragg-peak. Moreover we present a quantitative comparison between the depth dose profile obtained by a fast multi-slice T2-protocol with the result of Monte-Carlo dose Simulations (MCS) for a “normoxic” polymer gel [13, 14] modification featuring a reduced linear energy transfer (LET)-quenching. A 3-dimensional (3D) dose data-set is obtained for a mono-energetic proton beam with a voxel-size, 3 orders of magnitude ($10^3$) smaller than those available for 2D-arrangements of pin-point ionization-chambers used for the verification of treatment plans in intensity modulated radiotherapy with heavy ions [1].

2. Materials and methods

2.1 MRI
The high spatial resolution in parallel with acceptable SNR was achieved on a 7T human MR-scanner, equipped with a small sized (i.d. 90mm) strong gradient system (G=750 mT/m) and a linear TR-birdcage coil (i.d. 72 mm) [15].

2.1.1 High-resolution protocol
For investigating the spatial resolution in quantitative T2-mapping the point spread-function around a Boron wire (o.d. 100 µm) in a polymer gel irradiated with neutrons (T2=74ms) was evaluated using a high-resolution multi-slice-multi-echo sequence. The MR-measurement parameters for this high-resolution protocol are listed in the following: FOV:(30mm)$^2$, Mtx: 320$^2$, Voxel-size: 94x94x1000 µm$^3$, TE=10ms, 20 echoes.

2.1.2 3D-MRI-protocol
For investigating the 3D-dose response of several types of polymer gels (8 flacons in parallel) a protocol with reduced but still high spatial resolution was established with acceptable SNR (TM=11 min); FOV (50mm)$^2$, Mtx: 128x128x23, Vs: 547x547x1000 µm$^3$.

2.2 Polymer gels
Several sets of “normoxic” polymer gels with different additives for sensitivity and dose range modifications are manufactured. The presented data belongs to a variant using THPC [16] as oxygen scavenger, methacrylic acid (6% w/w) as monomer, gelatin (14%/w/w) and water.

2.3 Irradiation
Heidelberger Ion-beam-Therapy-center (HIT); Monoenergetic (E=59.8MeV) proton beam for human therapy; beam diameter: 6cm; $D = 0-4$Gy (plateau). The Monte-Carlo-simulations (MCS) are performed at fine raster (VS:500x500x500 µm$^3$) to resolve the fine Bragg-peak area.

3. Results

3.1 The full-width-half-maximum (FWHM) for the PSF in high resolution T2-maps (ps: 94x94µm$^2$) was calculated to be FWHM=214µm, assumed to be sufficiently high for the fine Bragg-peak.

3.2 The MR-protocol, optimized for measurement time and scan volume offered low T2-noise (ROI analysis: about 1-3%, see. also Fig. 1 for dose noise). The results concerning depth dose distribution and Bragg-peak enhancement ratio are sensitive to the polymer gel composition in specific oxygen scavenging. The measurement data for several different types of polymer gels exhibits also aging effects, when the normoxic polymer gels are stored at room temperature.
3.3 Best results are obtained for a THPC-scavenging polymer gel composition. The medium slice taken from the 3D-data-dose set (fig. 1b) evidences the possibility for 3D-high-resolution and low-noise dose-imaging for this polymer gel type. Using the optimized MR-protocol the depth dose distribution was calculated from calibrated data between 0-4 Gy using linear inter- and extrapolation for the proton beam. It is compared to the results of MCS (fig.1). The depth is corrected for the density of the polymer gel. MCS data is shifted in depth such that the Bragg-peak coincides with the dose maximum from experiment.

![Figure 1b: Dose image calculated from the medium slice of a 3D-T2-data-set after calibration.](image)

**Right:** polymer gel irradiated at a dose level of 4 Gy (plateau). The path of the profile for fig. 1 and 2 is indicated. The proton beam has entered the sample from left. The bright line at right indicates the Bragg-peak dose enhanced penetration depth.

**Left:** dose image of a sample irradiated at D = 2 Gy with opposite direction.

![Figure 1a: Depth dose profile as obtained from polymer gel data (fig. 1b). For comparison the results of Monte-Carlo-simulations normalized to the plateau-level at 10 mm depth are indicated.](image)

The depth dose distribution for an irradiation at 4 Gy is characterized by a slightly more flat distribution in the plateau regime with comparison to MCS. The reason is not yet clear. It might be related to a slight divergence of the proton beam, which is not included in MCS. The difference in Bragg peak is therefore sensitive to the normalization area of the MCS dose level.

The detected dose in the Bragg-peak (max.dose) is sensitive to the spatial resolution of MRI (pixel size). The result of voxel volume averaging connected to reduced MRI-measurement matrix size and subsequent increase in pixel size is plotted in fig. 2.

![Figure 2: Depth dose profiles (lines are spline interpolated) for different spatial resolutions (pixel size). The detected dose level in the Bragg peak is strongly underestimated when the pixel size is increased from ps=547 µm (black line) up to 2188 µm (green line).](image)
Reducing MR-scan resolution from ps: 547µm down to 1094 µm reduces the measured dose level by about 18% relative to the more accurate measurement (fig. 2). Edge enhancement in the polymer gel [11] was minimized by gel composition but could not be quantified.

4. Discussion/Conclusion

High spatial resolution in dosimetric imaging is critical for the accurate determination of the dose level in regions of high dose gradient as the Bragg-peak area. Using additional hardware components on a high-field human 7T-scanner T2-imaging can be implemented even at microscopic pixel size. Quantitative multislice-T2-micro-imaging at reduced spatial resolution and tolerable measurement time can be performed and applied to high-resolution 3D-polymer gel dosimetry for proton beam therapy, which poses high demands on spatial precision and signal/noise. The dose response of the specific polymer gel recipe is very sensitive to the oxygen scavenger concentration. A high resolution and pixel size of about 500 µm at minimum is necessary for an accurate measurement of the dose in the Bragg-peak regime. Otherwise the dose levels are underestimated in the Bragg-peak dose enhanced region due to spatial averaging of the dose in the voxel. The absolute accuracy in the Bragg-peak may be also be influenced by edge enhancement [11] in the polymer gel, by LET-quenching [12] and the temporal stability of the polymer gel dose response.

5. References

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