Descriptive analysis of MRI functional changes occurring during reduced dose radiotherapy for myxoid liposarcomas

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Objectives: Myxoid liposarcomas (MLS) show enhanced response to radiotherapy due to their distinctive vascular pattern and therefore could be effectively treated with lower radiation doses. This is a descriptive study to explore the use of functional MRI to identify response in a uniform cohort of MLS patients treated with reduced dose radiotherapy.

Methods: 10 patients with MLS were imaged pre-, during, and post-radiotherapy receiving reduced dose radiotherapy and the response to treatment was histopathologically assessed post-radiotherapy. Apparent diffusion coefficient (ADC), T2* relaxation time, volume transfer constant (Ktrans), initial area under the gadolinium curve over 60 s (IAUGC60) and (Gd) were estimated for a central tumour volume.

Results: All parameters showed large inter- and intra-subject variabilities. Pre-treatment (Gd), IAUGC60 and Ktrans were significantly different between responders and non-responders. Post-radiotherapy reductions from baseline were demonstrated for T2*, (Gd), IAUGC60 and Ktrans for responders. No statistically significant ADC differences were demonstrated between the two response groups. Significantly greater early tumour volume reductions were observed for responders.

Conclusions: MLS are heterogenous lesions, characterised by a slow gradual contrast-agent uptake. Pre-treatment vascular parameters, early changes to tumour volume, vascular parameters and T2* have potential in identifying response to treatment. The delayed (Gd) is a suitable descriptive parameter, relying simply on T1 measurements. Volume changes precede changes in MLS functionality and could be used to identify early response.

Advances in knowledge: MLS are characterised by slow gradual contrast-agent uptake. Measurement of the delayed contrast-agent uptake (Gd) is simple to implement and able to discriminate response.

INTRODUCTION

Soft tissue sarcomas (STS) represent a heterogeneous group of approximately 50 histological subtypes. Although in general sarcomas are considered to be radioresistant, studies suggest that myxoid liposarcomas (MLS) may show improved response rates following radiotherapy (RT) than other types of STS. A marked volume decrease, necrosis, and high control rates have been reported after a standardised pre-operative RT protocol (25 × 2Gy).1–4 The reason for this remarkable clinicopathological response is unknown but it is hypothesised that damage to the distinctive vascular pattern of MLS is a mechanism that may be relevant to radiosensitivity.2

Targeting tumour vasculature with lower than the standard dose levels could prove equally effective5–7; permanent radiation-induced damage to vascular endothelium and structure has been reported from doses as low as 10 Gy.5–8
The Dose Reduction of Preoperative Radiotherapy in Myxoid Liposarcomas (DOREMY) multicentre clinical trial aimed to investigate whether MLS can be effectively and safely treated with lower doses of radiation pre-operatively. The recently published results show that a treatment dose of 36 Gy achieved excellent local control rate (100%) and reduced wound complication rate (17%) providing an acceptable alternative for pre-operative radiotherapy in MLS.5

MRI is a particularly useful modality for the evaluation of STS, however, conventional MRI alone has a limited efficacy for assessing treatment-related response accurately when pathologic post-treatment changes share similar imaging characteristics with viable tumour.10,11 In clinical trials, volumetric measurements at MRI are commonly used to evaluate tumour response, however, poor correlations with patient outcomes have been demonstrated in heterogeneous patient cohorts.12,13

Changes in perfusion, cell proliferation and hypoxia often precede tumour size and morphologic alterations, and quantitative functional MR imaging techniques such as diffusion-weighted imaging (DWI), dynamic contrast-enhanced MRI (DCE-MRI) and T2* imaging are increasingly used to detect early changes.14–16 Reports on the pre-operative therapeutic (DCE-MRI) and T2* imaging are increasingly used to detect changes in tumour function in a cohort of patients with MLS.17,18 and quantitative DWI has shown promise to identify early response to treatment for STS.19 Given the histologic diversity of STS before and after treatment,2,13 measuring T2* may become relevant in monitoring treatment response, but the value of T2* as a prognostic factor of STS response, has not been explored. To date, functional MRI has not been applied specifically to MLS.

This is a pilot study which aims to describe early and late changes in tumour function in a cohort of patients with MLS receiving reduced dose RT pre-operatively and explore the use of MRI functional parameters to identify response. This cohort comprises a subset of patients from the DOREMY clinical trial. All patients were scanned employing a quantitative MRI protocol which was developed in one of the nine tertiary centres involved in the trial.

METHODOLOGICAL APPROACH

METHODS AND MATERIALS

10 patients (5 males, 5 females, median age = 41.5 years, age range = 21–53 years) with histologically confirmed MLS were scanned at 3T (Skyra, Siemens Medical Systems, Erlangen, Germany). The tumours were located in the thigh (n = 9) and gluteal (n = 1) regions. All scans were performed with the approval of the research ethics committee (REC reference number: 14/WA/1090).

Treatment protocol

Conformal RT or intensity-modulated RT were planned to deliver 36 Gy in 18 fractions, in daily fraction of 2 Gy, 5 days per week for an overall treatment time of 3.5–4 weeks.9

Repeated ultrasound-guided biopsies were performed on fractions 8 and 16 to assess the extent of tumour pathology changes (percentage viable cells, hyalinisation, proliferation and necrosis in proportion of viable cells) and alteration of vasculature. After the last (18th) fraction of 2 Gy patients were followed for 4–6 weeks before they underwent the definitive surgical resection. Tumour excision and the final histopathological assessment were performed 6–8 weeks post-RT, and used to assess response to treatment.

MR imaging protocol

MR imaging was performed pre-RT (visit 1), during RT at fractions 8 (visit 2) and 16 (visit 3), 4 weeks post-RT (visit 4) and 6 weeks post-RT (visit 5). For 2/10 patients, the final MRI visit was at 4 weeks post-RT (visit 4) for logistical purposes. The final MRI visit (the visit closer to the tumour excision) will be denoted as post-RT visit.

All patients were carefully positioned following the RT treatment set-up position. Table 1 details the imaging acquisition protocol.

Data post-processing and analysis

MR image processing and analysis were performed in MATLAB R2018b (The MathWorks, Inc., Natick, MA) and IDL (IDL 8.4, Boulder, CO). When necessary, non-rigid registration performed to compensate for patient movement and muscle deformation (MIRT – Medical Image Registration Toolbox, MATLAB, R2018b).20 High resolution DIXON at pre- and post-contrast and DWI data sets were aligned to the 2D multiecho GRE and DCE data sets and were resampled to match their spatial resolution (1.5 × 1.5 × 3 mm).

A pre-requisite in quantitative DCE-MRI is to ensure accurate pre-contrast variable flip angle (VFA) T1 measurements which are susceptible to errors due to spatial variations in flip angle caused by RF field (B1) inhomogeneity and are more pronounced at large field-of-views (FOVs) and higher magnetic field strengths (≥3T).21 Fat-only images from the 2-point Dixon GRE acquisitions for DCE-MRI were employed to correct the nominal flip angles. Flip-angle scaling factors were estimated for each voxel using fat (T1 = 370 ms at 3T) as the reference signal and interpolated (Delaunay triangulation, IDL) over the entire area of interest.22 The mean scaling factor was then calculated for the lesion only and applied to correct the nominal flip angle values used for pharmacokinetic analysis (Figure 1). For each patient, the median and the median absolute deviation of tumour ADC, T2* relaxation time, gadolinium concentration (Gd), initial area under the gadolinium curve over 60 s (IAUGC60) and volume transfer constant (Ktrans) maps were calculated over five central slices using in-house software (IDL applications - ADEPT and MRIW, The Institute of Cancer Research, UK), for visits 1 (pre-RT) and 2 (RT fraction 8) and for the final post-RT visit (visit 5 for 8/10 and visit 4 for 2/10 patients).

ADC and T2* were measured voxelwise employing Levenberg-Marquardt least-squares monoeponential fits. The Ktrans model parameter was estimated for all the enhancing voxels using the Tofts-Kety two-compartment model24 along with...
population-averaged arterial input function (AIF). A population-based AIF has been recommended for improved $K_{\text{trans}}$ repeatability and treatment sensitivity. The values were adjusted to incorporate changes in the enhancing fraction (EF) of the tumour as in. Voxels of non-convergence of the model or exhibiting no enhancement were removed when estimating tumour $K_{\text{trans}}$.

The concentration of the contrast agent ($[\text{Gd}]$) in each voxel was calculated quantitatively from $T_1$ values acquired from the downsampled, 2-point 3D gradient echo (GRE) based Dixon sequences before and after contrast administration. The $T_1$ values were calculated using the variable flip angle method and ($\text{Gd}$) measurements were made after DCE corresponding to late enhancement.

Table 1. Image acquisition protocol

|                      | TR/TE (ms) | Voxel size (mm$^3$) | Acquisition matrix | Reconstruction matrix | Receiver bandwidth (Hz/px) | Flip angle | b-values (s/mm$^2$) | Tumour coverage |
|----------------------|------------|---------------------|--------------------|-----------------------|----------------------------|------------|---------------------|----------------|
| Pre-contrast         |            |                     |                    |                       |                            |            |                     |                |
| High resolution      | 7/3.69     | 1.25 x 1.25 x 2     | 192 x 154          | 192 x 192             | 605                        | four $^\circ$/16$^\circ$ | N/A                | Full           |
| DW-EPI               |            |                     |                    |                       |                            |            |                     |                |
| 2D multi echo GRE    | 1120/77    | 1 x 1 x 4           | 128 x 104          | 208 x 256             | 2055                       | 90$^\circ$ | 50, 300, 600, 900   | Full           |
| Post-contrast        |            |                     |                    |                       |                            |            |                     |                |
| DCE-MRI 2-point      | 5.74/2.46  | 1.5 x 1.5 x 3       | 160 x 160          | 160 x 160             | 600                        | four $^\circ$/16$^\circ$ | N/A                | Central volume |
| 3D GRE Dixon         |            |                     |                    |                       |                            |            |                     |                |
| High resolution      | 73.69      | 1.25 x 1.25 x 2     | 192 x 154          | 192 x 192             | 605                        | four $^\circ$/16$^\circ$ | N/A                | Full           |
| DCE-MRI, Dynamic contrast enhanced-MRI; DW-EPI, diffusion weighted echoplanar imaging; GRE, Gradient echo. DWI, 2D multiecho GRE and DCE-MRI sequences were centered on a slice chosen by a specialist sarcoma radiologist to ensure targeting the section of the tumour with increased cellularity and to avoid areas of high fat content.

Tumours were delineated on subtracted images derived from the DCE data sets and the regions of interest (ROIs) were transferred to the corresponding parametric maps and combined to a volume of interest (VOI). The tumour volume within the VOI was also estimated from the volume of all voxels included in the VOI.

Descriptive statistics were computed to summarise all metrics from visits 1 (pre-RT), 2 (RT fraction 8) and from the final post-RT visit before tumour excision to explore early and late tumour functional changes within the course of RT. Differences between responders and non-responders were assessed using two-sided Wilcoxon rank sum tests. The percent changes relative to baseline (visit 1) were also reported and the relations between different metrics were investigated using Pearson’s product–moment correlation coefficient. For all statistical tests $p < 0.05$ was considered significant. Due to the small sample size, type II errors are more likely to occur and therefore no corrections for multiple testing were applied.

In this article, patients were classified as responders and non-responders according to their final histopathological assessment only: patients with 10% (or less) viable tumour were classified as responders. This stringent response criterion was employed in the run-in period of this trial to ensure patient safety in a dose reduction study. For completeness, the radiotherapy response was also assessed using the response evaluation criterion in solid tumors (v. 1.1) (RECIST 1.1) comparing pre- and post-treatment $T_2$ weighted images.

RESULTS

Five patients were evaluated as having stable disease and five as partial responders by RESICST 1.1 criteria comparing the pre- and post-treatment $T_2$ weighted images. Six patients were classified as responders and four as non-responders based on their final histopathological assessment.
Mean ± standard deviation of the maximum axial tumour dimensions at pre- and post-treatment is 89.8 ± 58.7 (range: 231–30) and 62.5 ± 40.4 (148–20) respectively.

Appearance of MLS at pre-treatment MRI
All MLS masses considered in our cohort were well-defined. On the non-enhanced \( T_1 \) weighted Dixon-based in-phase images (Figure 2, first row), the majority of the tumours appeared homogeneous and exhibited low signal intensities, due to the predominant myxoid component. High signal intensity foci within a low signal intensity mass in 2/10 MLS (Figure 2, second row) corresponded to the fat content of these tumours revealed in the final histopathological assessment.

One patient was contraindicated for gadolinium-based contrast agent on all MRI visits. The enhancement pattern of MLS was mostly heterogeneous as in Figure 2 (first and second rows) showing a gradual increase in enhancement following contrast administration (Supplementary Figure 1). In 2/9 patients who received gadolinium, tumours exhibited a homogeneous contrast uptake (Figure 2, third row).

MRI parameters and post-treatment changes
Table 2 summarises the mean ± standard deviation of the median MRI metrics of all the tumour volumes considered for responders and non-responders at baseline (visit 1), visit 2 and the post-RT visit. The use of a flip angle scaling factor (0.97 ± 0.16, mean ± standard deviation, range 0.61–1.26) enabled a larger number of voxels to be successfully modelled. Slow gradual contrast-agent uptake described by very low \( K_{\text{trans}} \) values. It was impossible to estimate \( K_{\text{trans}} \) for one patient in the responders group, as the two compartment model was a poor fit for the data, and therefore, this tumour was excluded from the pharmacokinetic analysis.

Large standard deviations of parameter estimates indicate large intersubject variability in the cohort. Comparisons showed significant differences between responders and non-responders at baseline (Gd), IAUGC60 and \( K_{\text{trans}} \) (\( p = 0.024, 0.024, 0.036 \), Table 2), but

| MRI parameters | Responders \( (n = 6) \) | Non-responders \( (n = 4) \) |
|----------------|----------------|----------------|
|                | Visit 1 | Visit 2 | Post-RT visit | Visit 1 | Visit 2 | Post-RT visit |
| ADC \((\text{x10}^{-5}\text{ mm}^2/\text{s})\) | 229.3 ± 47.9 | 251.8 ± 24.3 | 238.6 ± 27.7 | 227.2 ± 27.7 | 246.2 ± 29.8 | 193.7 ± 51.8 |
| \(T_2\) \((\text{ms})\) | 163.6 ± 75.7 | 145.9 ± 86.4 | 58.0 ± 25.0 | 64.2 ± 54.8 | 63.7 ± 47.0 | 33.8 ± 17.9 |
| \(\text{(Gd) (}10^{-3}\text{ mmol ml}^{-1})\) | 0.5 ± 0.2 | 0.42 ± 0.22 | 0.16 ± 0.13 | 0.09 ± 0.05 | 0.14 ± 0.08 | 0.10 ± 0.03 |
| IAUGC \((\text{mmol} \times \text{s})\) | 7.5 ± 3.0 | 7.0 ± 5.0 | 3.7 ± 2.1 | 1.8 ± 1.1 | 3.1 ± 0.9 | 3.3 ± 1.1 |
| \(K_{\text{trans}}\) \((\text{min}^{-1})\) (adjusted to EF) | 0.07 ± 0.02 | 0.06 ± 0.04 | 0.04 ± 0.03 | 0.02 ± 0.01 | 0.03 ± 0.01 | 0.03 ± 0.01 |
| Volume \((\text{cc})\) | 54.3 ± 40.8 | 43.3 ± 33.2 | 23.8 ± 19.7 | 64.7 ± 58.7 | 65.0 ± 60.0 | 40.5 ± 40.0 |

| RECIST 1.1 response classification | Partial response \( (n = 4) \) | Stable disease \( (n = 2) \) | Partial response \( (n = 1) \) | Stable disease \( (n = 3) \) |
|----------------|--------------------|--------------------|--------------------|--------------------|

ADC, apparent diffusion coefficient; RT, radiotherapy. Response classification according to RECIST 1.1 criteria. Number of patients considered for the calculations are clearly stated in the legend of Figure 3.

\(^*\) Denotes significant differences between responders and non-responders.

\(^*\) Please see Supplementary Table 1 for the RECIST 1.1 classification of all 10 patients separately.
In assessment of median Ktrans changes, overall reductions showed early uptake increases. Contrary to our expectations, responding tumours, whereas most non-responding tumours uptake (Gd), IAUGC60 were demonstrated for the majority of reductions from baseline for parameters reflecting contrast agent parameters for non-responders at baseline (Table 2). Early Figure 3c–e demonstrate the significantly lower median vascular (Figure 3b).

Table 3 lists the % change of all the parameter means for visit 2 and the post-RT visit when compared to baseline. In the responders group, statistically significant reductions of post-RT T2*, (Gd), IAUGC60 and Ktrans were demonstrated (p = 0.004, 0.015, 0.026, 0.030 respectively) when compared to the baseline values. On the contrary, all post-RT vascular parameters in the non-responders group increased and the changes from baseline were significantly different from responders [p = 0.048, 0.048, 0.036 for (Gd), IAUGC60 and Ktrans respectively]. There were significantly greater decreases in tumour volume in responders compared to non-responders after eight fractions (visit 2) (p = 0.038); non-responders exhibited smaller tumour volume reductions than responders post-RT but the difference was not significant.

The graphs in Figure 3 show the median parameter estimates and the corresponding median absolute deviation at visit 1, visit 2 and the post-RT visit. Considering patients individually, all tumours exhibited early ADC increases. For 3/6 responders, the ADC values further increased post-RT (Figure 3a) and 2 of them were classified as having a stable disease using RECIST 1.1 criteria.

Early T2* increases from baseline were observed for 3/4 non-responders and 3/6 responders, whereas T2* reductions were consistently observed post-RT for both response groups (Figure 3b).

Figure 3c–e demonstrate the significantly lower median vascular parameters for non-responders at baseline (Table 2). Early reductions from baseline for parameters reflecting contrast agent uptake ((Gd), IAUGC60) were demonstrated for the majority of responding tumours, whereas, most non-responding tumours showed early uptake increases. Contrary to our expectations, (Gd) and IAUGC60 were not significantly correlated.

In assessment of median Ktrans changes, overall reductions and increases from baseline were consistently observed among responders and non-responders respectively. One responder exhibited an initial increase in median IAUGC60 and Ktrans but a steep decrease in these parameters followed (Figure 3d and e, double red arrow). A significant positive correlation was demonstrated between Ktrans and IAUGC60 (r = 0.59, p = 0.0013) but all other parameter associations did not reach statistical significance (p > 0.05).

**DISCUSSION**

In this descriptive study, we analyse the evolution of MRI-derived functional parameters in a uniform cohort of MLS patients from the DOREMY clinical trial. We have described early and late tumour functional changes seen with MRI.

MLS could be indistinguishable from cystic lesions and other soft-tissue masses using conventional MRI. However, unlike cysts, MLS in this cohort showed marked contrast uptake in agreement with previous reports and gradual enhancement potentially resulting from the myxomatous large interstitial compartments and fibrous tissue within MLS. The slow gradual enhancement observed (Supplementary Figure 1) was a characteristic for all MLS in our cohort and therefore we expect the vascular parameters to be the most relevant to study response.

The baseline ADC values in the present study are higher than the values reported previously, due to the myxoid matrix of MLS. The baseline ADC values and their post-treatment changes were not different between the two response groups. STS may have areas of fat, necrosis, viable tumour and haemorrhage with different diffusion properties suggesting that tissue integration may obscure ADC changes with treatment. ADC increases post-RT observed in two responding patients assessed as having stable disease by RECIST 1.1 criteria is in broad agreement with a study by Winfield et al.

T2* relaxation time is an imaging biomarker that has shown an association with tumour oxygenation as well as a dependency on tissue structure. Our observations support T2* dependency on tissue structure; tumours with different tissue content exhibited different T2* change behaviour (Figure 3). The wide range of T2* baseline values found is indicative of the inter-
intratumoral heterogeneity of MLS in this cohort. Low T2* variability among MLS have been previously reported, however, measurements concern a central slice excluding areas of necrosis and haemorrhage. Our observation of statistically significant T2* decreases post-RT for responders is potentially related to treatment-induced fibrosis and sclerosis. Non-responding tumours exhibited lower baseline T2* values and therefore there has less scope for a proportional T2* reduction post-RT compared to the responding tumours.

The baseline values of the quantitative vascular MRI parameters reported herein show promise in the prediction of treatment response. Baseline $K_{\text{trans}}$ has been previously found to be a good marker for the prediction of early soft-tissue sarcoma response. Our findings suggest that MLS with higher perfusion and permeability at baseline have higher blood supply indicating better oxygenation, and therefore greater radiosensitivity and better response. In contrast, Huang et al found lower baseline perfusion and permeability for optimally responding tumours, however, the soft-tissue sarcoma patient cohort was heterogeneous and subtypes assessments were not performed. Decreases of $K_{\text{trans}}$ early in the RT course and post-RT of the responding tumours agree with other DCE-MRI clinical and pre-clinical studies of soft-tissue sarcomas. The increase of $K_{\text{trans}}$ in
the non-responding tumours may relate to underline functions that support increased perfusion for future growth.\textsuperscript{18}

IAUGC60 and model-based $K_{\text{trans}}$ show an association for all patients (Figure 3d and e) and this observation agrees with previous studies reporting strong correlations between the two parameters.\textsuperscript{38,46,47} Therefore, IAUGC60 is often the parameter of choice clinically due to its robustness and lack of assumptions. However, simulations performed by Walker-Samuel et al\textsuperscript{16} revealed that IAUGC is a mixed metric and should not be used as a surrogate measure of $K_{\text{trans}}$.

Similar to IAUGC60, baseline (Gd) was able to discriminate response. In contrast to pharmacokinetic modelling, (Gd) measurement for delayed contrast-agent uptake is a simple and easy method to implement; it relies on T1 measurements and avoids challenges associated with rapid acquisitions and modelling.

Against our expectation, we did not find an association between (Gd) and IAUGC60 and therefore several sources of measurement error were considered. Flip angle accuracy is of paramount importance in determining the accuracy of quantitative DCE-MRI. It affects the baseline T1 and hence the calculation of the contrast agent uptake and vessel permeability. Flip angle non-uniformities arise from B1 inhomogeneities which are more pronounced at large magnetic fields (≥3T) and large FOV.\textsuperscript{22} In the present study, we corrected our DCE-MRI quantitative measurements over the ROI by applying a scaling factor to the flip angle derived using the signal from fat as a reference.

DCE-MRI parameter estimations may be affected by blood inflow, and these effects cannot be completely excluded in this cohort. Other potential sources of error (non-steady state of the longitudinal magnetisation, receiver gain changes between low and high flip angle acquisitions and adequacy of the spoiled GRE equation\textsuperscript{27} to characterise our data) were examined and found that they are unlikely to have affected our T1 measurements.

Early volume changes were significantly different in responding MLS suggesting that RT-induced size reductions occur early within the treatment course.47,48,49 But their cohort was heterogeneous comprising soft-tissue sarcomas of different histological subtypes. Large treatment-induced size reductions have been reported for MLS in several studies\textsuperscript{43,46,49} and the response has been related to tumour volume changes.\textsuperscript{13}

There were limitations to the study. First, the sample size of the cohort is small, but constitutes a homogenous patient population. Nevertheless this study contributes important information, as only a limited body of literature assesses the value of functional MRI in discriminating STS response to radiotherapy, and none of those studies are dedicated to a uniform cohort of MLS. In addition, small studies like ours aim to create further hypothesis to be tested in larger studies. The observation of no significant changes of ADC could be attributed to the small sample size and also the fact that all parameters were calculated including the entire tumour volume considered. A more sophisticated analysis excluding areas of necrosis and fat could potentially prove useful in highlighting the value of ADC in discriminating response of MLS as suggested in other STS studies.\textsuperscript{19,36,37,50} Another limitation of the study is the lack of repeatability evaluation for the parameters considered. However, good ADC, T2*, IAUGC60 and $K_{\text{trans}}$ repeatability has been demonstrated in previous reports suggesting the implementation of such parameters with a high level of confidence.\textsuperscript{27,35,31,32} We acknowledge there are risks associated with the administration of multiple doses of Gd-based contrast agents (nephrogenic systemic fibrosis and retention in a range of tissues and organs). However, all patients received contrast agent in our cohort were administered a macrocyclic Gd-based contrast agent where the risks are much lower compared to their linear counterparts.\textsuperscript{51} Moreover, all individuals were at a low risk of an adverse event and therefore, the cohort was expected to experience no risks in addition to those for standard MRI scanning with administration of Gd-based contrast agent.

In conclusion, in this pilot study we have described functional changes in a homogenous cohort of MLS patients receiving reduced dose RT. Vascular parameters (Pre-treatment (Gd), IAUGC60 and $K_{\text{trans}}$) were significantly higher for responders and their predictive value merits further investigation. MLS are heterogeneous lesions, characterised by a slow gradual contrast-agent uptake. The delayed (Gd) is a suitable descriptive parameter, relying simply on T1 measurements pre- and post-contrast agent injection. Early changes to tumour volume, vascular parameters ((Gd), IAUGC60 and $K_{\text{trans}}$) and T2* have potential in identifying response to treatment. Further work is required to describe tumour heterogeneity and ensure functional differences are not obscured by integration of functional parameters over the tumour volume.

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