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Soft Tissue Sarcoma Stiffness and Perfusion Evaluation by MRE and DCE-MRI for Radiation Therapy Response Assessment: A Technical Feasibility Study

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Abstract

Soft tissue sarcomas are a rare and heterogeneous group of malignancies that present significant diagnostic and therapeutic challenges. Patient stratification based on tumor aggressiveness and early therapeutic response based on quantitative imaging may improve prediction of treatment response and the evaluation of new treatment strategies in clinical trials. The purpose of this pilot study was to determine the technical feasibility of magnetic resonance elastography (MRE) and dynamic contrast-enhanced (DCE) MRI for the evaluation of sarcoma stiffness and perfusion in 9 patients with histologically confirmed sarcoma. Additionally, we assessed the feasibility of utilizing MRE and DCE-MRI for the early evaluation of response to radiation therapy in 4 patients to determine the utility of further evaluation in a larger cohort study. Tumor size, stiffness, and perfusion parameters all decreased from baseline at the time of the pre-surgery or follow-up MRI, and results were compared to pathology or conventional imaging. MRE and DCE-MRI may be useful for the quantitative evaluation of tumor stiffness and perfusion, and therapy response assessment in soft tissue sarcomas.

1. Introduction:

Sarcomas are a rare group of malignancies comprised of over 50 different histologic subtypes (Helman and Meltzer, 2003). Sarcoma treatment is challenging due to the heterogeneity of this disease group. Anatomic imaging has become a critical component in the differential diagnosis, radiotherapy treatment planning, surgical planning, and treatment response assessment of sarcomas. Although change in tumor size has traditionally been used to demonstrate response to treatment, only a minority of sarcomas demonstrate significant reduction in size in response to treatment and internal necrosis and hemorrhage can cause enlargement of the tumors (pseudo-progression) even with a favorable treatment response (Wortman et al., 2016). Pathologic response is associated with local control and overall

survival in sarcoma patients. However, in some patients with locally advanced disease, resection of the tumor to assess response is not possible. In addition, sarcoma chemotherapy is toxic and only the minority of patients have significant pathologic response so many patients unnecessarily receive toxic, ineffective therapy. A non-invasive imaging technique to allow early assessment of treatment response could allow patient-specific treatment modifications and a more rapid investigation of novel therapeutics, or guide efforts for dose-escalation to poorly-responding regions of the tumor to improve outcomes for these patients.

Magnetic resonance elastography (MRE) is a noninvasive MR imaging technique capable of quantifying tissue mechanical properties (Muthupillai et al., 1995). Tissue stiffness is significantly altered with the development and progression of cancer, and has been assessed with MRE to detect and characterize malignant tissue, evaluate response to therapy, and investigate the underlying tissue biomechanics of tumors (Pepin et al., 2015a, Pepin et al., 2013, Juge et al., 2012, Li et al., 2014, Venkatesh et al., 2008). Dynamic contrast-enhanced MRI (DCE-MRI) is a technique sensitive to changes in the tissue microvasculature and can both qualitatively and quantitatively assess physiologic parameters related to tissue perfusion (Essig et al., 2013a, Essig et al., 2013b). DCE-MRI is used for staging and response assessment of soft tissue tumors and may help distinguish recurrence and radiation-induced soft tissue edema (Taylor and Reddick, 2005). DCE-MRI has previously been applied in soft tissue sarcomas and has been found to correlate with histologic response following preoperative chemoradiotherapy (Huang et al., 2016, Meyer et al., 2013, Xia et al., 2017).

Our hypothesis is that MRE, which has not been used in sarcoma patients, in conjunction with DCE-MRI, can be used to quantify tumor stiffness and perfusion in sarcomas. In this initial feasibility study, tumor stiffness, perfusion, and volume were calculated in an initial group of patients in order to develop the technique, and then were evaluated pre- and post-radiation therapy and compared with pathology at the time of surgical resection in a subset of patients in order to determine the feasibility of comparison with clinical response. The long-term goal of this work is to establish change in tumor stiffness and perfusion determined by MRE and DCE-MRI as biomarkers for early therapeutic response.

2. Methods:

2.1. Subject Selection

A total of 13 patients and 6 normal controls were recruited for this IRB approved study and written consent was obtained during the time period between January 2016 and July 2017. The inclusion criteria were age ≥ 18 years, histological confirmation of Ewing sarcoma, Rhabdomyosarcoma, or soft tissue sarcoma, and tumor diameter of at least 5 cm. Alternative criteria for the normal controls was no previous history of sarcoma. Exclusion criteria included contraindications for MRI, contraindications to the contrast agent (allergy or renal insufficiency), and tumors arising mostly from bone. Subjects were divided into two groups for the study. Group 1 was the technical development patient cohort ($n = 15$; $n = 9$ patients and $n = 6$ normal controls) and subjects were scanned during a single time point. The normal controls received MRE only and DCE-MRI was not performed to avoid unnecessary contrast agent administration. Group 2 ($n = 4$) was the longitudinal response assessment patient cohort, and subjects were scanned at multiple time points to determine feasibility of using

MRE and DCE-MRI to assess response to radiation therapy. Additional inclusion criteria for Group 2 required patients to be receiving radiation therapy at our institution, the sarcoma must be newly diagnosed or recurrent (>1 year post-treatment), and that baseline MRE and DCE-MRI occurred no more than 21 days prior to the start of treatment.

2.2. MRE

MRE essential involves three steps: 1) application of small amplitude vibrations to the tissue of interest, 2) imaging of the response of tissue to the stimulus, and 3) mathematical processing of the response to quantify tissue stiffness (Muthupillai et al., 1995). MRE is well established and clinically utilized for applications in the liver (Serai et al., 2017) and is under investigation for research applications in a variety of other sites including brain, breast, prostate, and tumors (Pepin et al., 2015b). One of the unique challenges of the application of MRE in sarcomas is the variable anatomic location, size, and heterogeneity of these tumors. Challenges related to the application of shear waves in sarcomas arise due to the varied anatomic location of these tumors, and have implication for the selection of the shear wave driver to apply the vibrations, placement of the driver, and image acquisition parameters. This feasibility study focused on the development of MRE strategies in patients with sarcoma, depending on anatomic location of the tumor.

MRE was performed on a 3.0T MR imaging system (Signa, GE Healthcare, Waukesha, WI) for the normal controls. MRE shear wave drivers, vibration frequency, and experimental set-up involving immobilizations for radiation oncology treatments were evaluated. In normal volunteers and pilot patients, MRE vibration frequencies ranging from 60-120 Hz were tested in representative anatomic locations of soft tissue sarcomas including upper and lower extremities, pelvis, and abdomen. Shear wave penetration, MRE acoustic driver selection, driver positioning, and set-up were assessed, and a protocol was developed for anatomic sites described below. For Group 1 (n = 9 patients), MRE was performed using a 3.0 T MR imaging system (Discovery MR750w, GE Healthcare, Milwaukee, WI) during a clinically indicated MR exam for each patient that included T1-, T2- and post-contrast T1-weighted sequences. Due to the variable anatomic location of sarcomas, acquisition protocols were divided into regional anatomical locations including upper and lower extremities, thorax, and abdomen/pelvis. Feasibility testing was performed in the normal controls in each of these anatomic locations. Radiofrequency coil selection depended on anatomic location of the tumor and included a cardiac coil, body coil, and posterior array embedded within the patient table (Geometry Embracing Method “GEM” Suite, GE Healthcare, Milwaukee, WI). MR image acquisition was acquired with the patient in radiotherapy treatment position with their MR-compatible immobilization device when available. Mechanical waves at a frequency of 60 Hz were induced in the target area using custom-built flexible passive pads or a flexible ball connected to an acoustic actuator located outside the scan room (Resoundant Inc, Rochester, MN). The driver was secured on the patient using a flexible strap to ensure constant contact with the body during imaging (Figure 1).

The resulting shear waves produced in the tissue were imaged using a gradient-echo MRE pulse sequence with motion-encoding gradients synchronized to the applied vibration. MRE representative parameters: 3D-GRE acquisition; repetition time/echo time (TR)/(TE) =

24.1/20.3 ms; field of view (FOV) = 24-36 x 24-36 cm²; 128×128 image matrix; 24-40 partitions with 3-mm thickness; 3 phase offsets; 4-9 minutes. To save TE and gradient heating, fractional motion encoding gradients (MEGs) were employed with typical motion encoding values of 18-20 π -radians/ μ m. The MEGs were single sided applied in the x, y, and z directions with three equally spaced phase offsets, sampled over one period of the applied 60 Hz motion. Exact parameter selection including field of view, image slice orientation, and overall acquisition time varied between patients depending on tumor location.

MRE post-processing was performed by taking the curl of the 3D displacement field and performing a 3D local frequency estimation (LFE) inversion with directional filtering (Manduca et al., 2001). The 3D directional filter was applied with cutoff frequencies of 2 and 128 cycles/FOV in order to remove interference patterns due to reflection and refraction of the shear waves (Manduca et al., 2003). LFE was selected due to its relative insensitivity to noise and signal-to-noise ratio compared to other inversion techniques including a direct inversion of the Helmholtz equation. The result is a quantitative estimate of the material stiffness equal to $\lambda^2 f^2 \rho$, where λ is the shear wavelength (m), f is the frequency of the applied mechanical vibrations (Hz), and ρ is the density of the material which is assumed to be that of water, or 1000 kg/m³. For Group 1 patients, stiffness values were reported for manually drawn regions of interest (ROI). The presence of shear waves in the tumor was confirmed visually. For Group 2, Radiation Oncologist-defined gross tumor volumetric (GTV) contours from the treatment planning MRI were used to generate a volumetric mask for stiffness and perfusion calculations. Using commercial software (MIM Software Inc., Cleveland, OH), the baseline MRE image was rigidly registered to the anatomic sequences. The GTV contour was then propagated using deformable registration for mask generation at additional imaging time points, where contours were reviewed by an expert Radiation Oncologist. GTV contours were cropped out from bone in patients where both bony and soft tissue disease were present. For MRE masks, the GTV contours were uniformly contracted by 2 mm for smaller volumes (e.g. extremities) and 5 mm for larger volumes (e.g. pelvis, retroperitoneal, and head and neck) to avoid regions near the boundaries of the tumor and surrounding tissues that may have partial-volume MRE processing artifacts. Results were reported as mean stiffness $\pm$ standard deviation (range).

2.3. DCE-MRI

The DCE-MRI acquisition used in this study was based on a 3D fast spoiled gradient-echo (SPGR) acquisition with view sharing (Haider et al., 2008). A gadolinium-based contrast agent (Gadavist, Bayer Health Care Pharmaceuticals, Whipping NY) was administered at a dose of 0.1 ml/kg and flow rate of 3 ml/s followed by a 20 ml saline flush using a mechanical power injector. Imaging parameters included: TR/TE = 24.1/20.3 ms; FOV = 24-36 cm²; sampling resolution (in-plane matrix) = 192×256, interpolated to 256×256; sagittal plane; 38-128 slices with 1.5 mm thickness; field of view = 36 cm²; 2D SENSE acceleration = 2.5 (L/R) $\times$ 1.5 (S/I); 12° flip angle; 15-31 time frames; 6.6 s frame time; 3-5 min acquisition time, and 20-25 s temporal footprint (the duration over which any views used for a single image are acquired)(Haider et al., 2008).

For Group 2, masks were generated using the process described above without uniform contraction. Quantitative perfusion parameters were estimated by fitting the Tofts-based model to the acquired data with non-linear regression that utilizes the variable projection (VARPRO) technique to calculate the pharmacokinetic parameters K^{trans} [min^{-1}] and k_{ep} [min^{-1}] (Kargar et al., 2018). K^{trans} is the volume transfer constant between the blood plasma and extravascular extracellular space and k_{ep} is the rate constant. The VARPRO technique provides a robust and efficient numerical optimization strategy to determine the non-linear least squares estimates of the perfusion parameters. In this work, MR signal intensity was used for perfusion model fitting. A patient-specific arterial input function (AIF) was selected from an artery within the FOV using a 3×3 voxel ROI chosen from within the lumen of the vessel, and depended on anatomical location. All computations were performed using MATLAB (2016a, Mathworks, Natick, MA). Quantitative results were reported as mean $\pm$ standard deviation (range).

2.4. Therapy response feasibility study

The first four patients from an ongoing study were included in this analysis (Group 2) to assess the feasibility of using MRE and DCE-MRI to assess radiation treatment response. Imaging response results were compared with pathological response ($n = 3$) or with post-treatment/follow-up imaging ($n = 1$). MR acquisition protocols described above were used at pre-treatment (baseline), post-treatment/pre-surgery, and at follow-up (Figure 2). MRE was acquired at three mid-treatment time points (day 5, day 15, and end of RT). DCE-MRI was not performed mid-treatment to minimize contrast administration. Patients were imaged using their radiation therapy immobilizations to ensure a reproducible setup.

Therapeutic response was assessed using established clinical metrics including RECIST criteria, volumetric measurements and pathology. Change in GTV volume was calculated using commercial software (MIM Software Inc., Cleveland, OH) from the baseline volume and contours mapped to the follow-up imaging that were modified by the Radiation Oncologist. Following definitive surgery, pathologic evaluation included histologic assessment performed by an experienced pathologist. The surgical specimen was kept oriented following excision and then sectioned per standard of care. Photographs of the oriented sections were obtained and locations of samples taken for tissue mapping were recorded on the photograph by research and pathology staff. Pre-surgical imaging was used to subdivide areas of the physical tumor specimen for pathology assessment correlations with imaging. For example, if a section of the MRE results appeared particularly soft or stiff, the pathologist would review the corresponding sub-region on the physical specimen and provide quantitative percentages of fibrosis, necrosis, and viable tumor. Percent viability, percent necrosis, and percent fibrosis were reported for each tissue block by an experienced musculoskeletal pathologist and visually displayed on the photographed specimen using a color-coded pie chart representing the reported percentages of necrosis, fibrosis, and viable tissue. Correlations between imaging and pathology results were visually assessed.

3. Results:

Patient demographics, tumor type, and imaging time point are summarized in Table 1. Fifteen patients were recruited from January 2016 to June 2018 (n = 11 at a single time point, n = 4 at multiple time points to evaluate response to radiation therapy). DCE-MRI was not performed in three patients in Group 1 because contrast administration was not clinically indicated (n = 2) or due to technical difficulties (n = 1). Patient demographics included mean age of 61 years (range: 38-83), n = 11 female, and median tumor volume of 188.9cc (range: 32.3-22,567 cc). The additional time (about 15-20 minutes) for both DCE-MRI and MRE exams was well tolerated in all patients.

Sarcomas are very heterogeneous tumors in anatomy, stiffness and perfusion, with stiff and soft regions (Figure 3) as well as enhancing and non-enhancing regions (Figure 4). In addition to intra-tumor heterogeneity, sarcomas stiffness and perfusion demonstrated inter-patient heterogeneity. Mean tumor stiffness across all patients was 2.37 ± 1.49 kPa (range: 0.89 – 6.3 kPa). Mean K^{trans} and k_{ep} values were $1.62 \pm 1.44 \text{ min}^{-1}$ (range: 0.33 – 5.5 min^{-1}) and $2.60 \pm 1.75 \text{ min}^{-1}$ (range: 0.90 – 7.05 min^{-1}) respectively.

Change in tumor stiffness and perfusion following radiation therapy was evaluated in 4 patients and compared to clinical metrics of response including RECIST measurements, change in GTV volume, and pathology (Table 2). Treatment type for each patient is indicated in Table 2, where patient #12 received radiation therapy alone (proton therapy) and patients 13-15 received radiation therapy + surgery +/-chemotherapy. In the case of definitive proton therapy (#12), treatment response was determined by the physician after the second follow-up MRI to be progressive disease based on the presence of new metastases. In patient #13, tumor stiffness and perfusion parameters decreased following radiation therapy, corresponding to a decrease in tumor volume and the presence of necrosis (Figure 5 a-g). To display the pathology results, pie charts were created for each sample which was mapped to the specimen photograph at the time of sectioning (Figure 5 h).

4. Discussion:

In this feasibility study, we demonstrated acquisition of MRE and DCE-MRI in 13 patients with sarcoma at various anatomical locations including upper and lower extremities, chest wall, and pelvis. In four of these patients, imaging was performed before, during, and after radiation therapy, demonstrating feasibility of using MRE and DCE-MRI to quantitatively evaluate changes in tumor stiffness and perfusion after treatment. MRE and DCE-MRI were technically feasible in every case. We anticipated technical challenges related to varying anatomic location of the tumors; however application of shear waves was successful in all cases. The most straightforward application of shear waves was for tumors located in the extremities. Deep seated tumors in the pelvis were slightly more challenging and shear wave attenuation could lead to poor results in patients with a large body habitus. Challenges occurred with particularly large tumors (>2000 ml), where it was difficult to induce adequate shear waves throughout the entire tumor. In these cases, regions of interest were drawn only to include areas of adequate shear wave amplitude (assessed visually), which is the standard of practice in other applications of MRE including the liver (Venkatesh et al., 2013a).

Regional changes in tumor stiffness and perfusion parameters were observed and compared to pathological indices including the presence of necrosis, fibrosis, and viable tumor, demonstrating the feasibility of this workflow. Future work is needed to determine how stiffness varies with pathologic response to radiation therapy in sarcomas.

This study is the first application of MRE techniques to assess early response to radiation therapy in sarcoma patients including correlation of imaging response results with the gold standard of pathological response. The results demonstrate that changes in sarcoma tumor stiffness and perfusion parameters following radiation therapy can be quantified and compared with pathological findings. We quantified a decrease in tumor stiffness following radiation therapy in all 4 patients. In two cases, there was a large decrease in stiffness (49% and 71%), and the percent necrosis at time of surgery was 40 and 49%, respectively. In the two cases with a small change (10%), a small amount of necrosis was present at surgery (12%) and the patient without surgery demonstrated progressive disease based on radiographic findings. These results suggested that change in tumor stiffness may be correlated with clinical metrics of response. This pilot study demonstrated initial clinical feasibility and trending results that will warrant further investigation to determine the clinical significance and to assess tumor stiffness change as an indicator of early treatment response and/or predictor of patient outcome following radiation therapy.

Our results are also consistent with previous studies investigating early chemotherapy response in animal models, where a decrease in tumor stiffness was indicative of response to therapy (Juge et al., 2012, Pepin et al., 2013, Li et al., 2014). Alternatively, the effect of radiation therapy on mouse brain tumors was explored using MRE and found that the mechanical properties of the brain tumor did not change significantly following radiation therapy (Feng et al., 2016). Histology and change in volume were not reported in the preclinical study, making it difficult to compare treatment effect between these studies. In our study, in addition to percent necrosis which is a clinical indicator of response to therapy, percentage of viable tumor and fibrosis were also reported. The presence of fibrotic tissue is expected to affect the overall tumor stiffness (Yin et al., 2007). The effect of the percentage of viable tumor cells is less understood. Cancer cells are softer than normal cells, but the overall rigidity of the tumor may be due to stiffening of the stroma (Alibert et al., 2017). Future work is needed to discern the effect of radiation therapy on each component and the overall change in tumor mechanical properties. Additionally, correlation of stiffness and perfusion properties with other histologic findings such as tumor grade and genetic subtype should be explored as well as comparison with additional imaging techniques such as diffusion-weighted imaging (Pepin et al., 2018).

Volumetric response is variable in sarcomas following treatment and in some published studies an initial increase in volume can be observed (Canter et al., 2010) despite eventual pathologic response. In all cases in our series, a decrease in tumor volume was observed. The patient treated with definitive RT had minimal reduction in stiffness (10%) and progressed almost immediately following therapy. Radiation-induced soft tissue edema also makes it difficult to distinguish residual/recurrent tumor, and DCE-MRI may be useful in discriminating recurrent tumor versus radiation effects and post-surgical changes (Taylor and Reddick, 2005, Del Grande et al., 2014). We observed a decrease in perfusion parameters

following radiation therapy in all 4 patients including one patient with a very low presence of necrosis at the time of surgery, suggesting minimal treatment effect, and a second patient with disease progression but no pathology results available. A decrease in K^{trans} is consistent with previously reported results following chemotherapy and/or radiation therapy in sarcomas (Huang et al., 2016), but did not provide any additional information beyond change in tumor stiffness assessed with MRE to predict necrosis at the time of surgery.

There are a few limitations of the current study. In order to accurately and reliably assess response to therapy using MRE, the repeatability coefficient for MRE of tumors must be determined. MRE is highly reproducible, repeatable, with high inter-observer agreement, and is reproducible across different manufacturers (Lee et al., 2014, Venkatesh et al., 2013b, Hines et al., 2010). Ongoing work will evaluate the repeatability coefficient of MRE in sarcoma. Additionally, there are some limitations related to the resolution of MRE due to the dependency not only on imaging resolution but also the shear wavelength. However, several publications have demonstrated the utility of MRE to detect intra-tumoral consistency and improving the spatial resolution of MRE is an active area of research (Hughes et al., 2015, Bruix and Sherman, 2005). Inclusion criteria for this study included a minimum tumor diameter of 5 cm to allow for a decrease in tumor volume with treatment. Previously published studies in the brain have used a minimum diameter of 2 cm. The minimum tumor volume at which tumor stiffness can be reliably assessed is not well defined and depends on various parameters including vibration frequency and tumor location, and therefore future work is needed to better understand tumor size limitations for MRE applications. The reproducibility of DCE-MRI is more difficult to assess due to the requirement of an additional dose of the contrast agent, however a previous study in human muscle and tumors reported the ability to detect changes greater than 14-17% (Galbraith et al., 2002). Additionally, in the imaging/pathology comparison, the pathologic specimens were only grossly correlated with the imaging results. While the tumors were kept oriented following resection, sectioning was performed at the discretion of the pathologist and was not always in the same plane as the imaging. Future work will help define an improved workflow and potentially improved registration between the pathology and imaging results.

5. Conclusion:

In summary, we have quantified stiffness and perfusion parameters in sarcomas with the long-term goal of using MRE and DCE-MRI to evaluate response to radiation therapy. The ability of MRE and DCE-MRI to accurately assess early response is promising in its potential to efficiently evaluate novel and targeted therapies and help move towards more individualized treatment options for patients with sarcoma. Continued research in the application of MRE and DCE-MRI in sarcoma is critical and would provide the potential to individualize therapeutic decisions based on patient-specific response to therapy.

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Figure 1:

(A) Selection of acoustic drivers used for sarcoma MRE. From left to right: small pad, flexible abdominal, and ball driver. (B) Example driver selection, driver placement, and radiation therapy immobilization for a patient with a sarcoma of the thigh. Ball driver is positioned in close proximity to the tumor and secured in place using a strap.

Figure 2:

Sample MR imaging timeline for patients enrolled in longitudinal study. Clinically indicated tests shown in dark grey and research only sequences in light grey. Results from the pre-surgery imaging are used to inform additional sampling of the tumor at the time of pathology based on regions of heterogeneity observed, indicated by the dotted line.

Figure 3: Stiffness heterogeneity in a pelvic myxoid liposarcoma (Patient #7). Images showing the MRE magnitude (a,d), masked shear wave (b,e) and masked elastogram (c,f) for two sagittal slices (top and bottom rows) through the tumor. (g) Histogram of stiffness values with mean = 1.60 kPa, standard deviation = 0.47, kurtosis = 3.07, and skewness = 0.53.

Figure 4: Perfusion heterogeneity in a pelvic myxoid liposarcoma (Patient #7). Images showing the anatomic heterogeneity on a T2-weighted image (a,c) and K^{trans} (b,d) for a superior (a,b) and inferior (c,d) axial slice of the tumor. (e) Histogram of K^{trans} values with mean = 0.35 min^{-1} , standard deviation = 0.29, kurtosis = 4.88, and skewness = 1.13.

Figure 5:

Change in tumor stiffness and perfusion following radiation therapy in a calf myxoid liposarcoma (patient #14) from baseline (top row) to 3 months post-radiation therapy (bottom row). Tumor volume decreased 12% from baseline (a) to post-therapy (d) while tumor stiffness decreased 71% (3.4 kPa to 1.0 kPa)(b,e) and perfusion decreased 47% (1.16 min^{-1} to 0.61 min^{-1})(c,f). Overall, 49% necrosis, 29% fibrosis and 23% viable tumor was present at the time of surgery (g,h). Representative sections shown in (g) containing mostly viable tumor (V), necrosis (N), and fibrosis (F), corresponding to regions on the gross pathology image (h) as indicated by the white arrows and labels. Percent viable tumor (white), necrosis (black) and fibrosis (grey) is shown in a pie chart for each tumor section sampled and mapped to the pathology image (black box).

Table 1:**Subject Demographics and Clinical Pathological Characteristics**

Group	Patient #	Sex	Age (years)	Location	Histologic Subtype	Tumor Grade	Volume (ml)
1	1	F	64	Right retroperitoneal	Leiomyosarcoma	Inter	NA
1	2	F	54	Right calf	Synovial sarcoma	Inter	NA
1	3	M	38	Right anterior chest wall	Pleomorphic liposarcoma	High	32.3
1	4	F	55	Left tricep	Undifferentiated Pleomorphic sarcoma	High	188.9
1	5	F	70	Right proximal tibia	Myxofibrosarcoma	High	53.4
1	6	M	55	Left tricep	Ewing sarcoma	NA	25.9
1	7	F	38	Right hemipelvis	Myxoid liposarcoma	Low	2705
1	8	M	75	Right iliacus	Sclerosing variant of well-differentiated liposarcoma	Low	160.3
1	9	F	52	Right thigh	Angiosarcoma	NA	218.5
1	10	F	67	Retroperitoneal/Chest wall	Undifferentiated pleomorphic sarcoma	High	138.5
1	11	F	79	Right axilla	Pleomorphic sarcoma	High	113.2
2	12	M	83	Right paraspinal	Undifferentiated spindle cell sarcoma	Inter	253.2
2	13	F	55	Left distal thigh	Myxoid liposarcoma	Low	479.8
2	14	F	62	Left calf	Myxoid liposarcoma	Inter	252.8
2	15	F	65	Left posterior thigh	Myxofibrosarcoma	Low	22567

Abbreviations: M, male; F, female; Inter, intermediate; NA, not available or not applicable

Table 2:

Percent decrease in tumor parameters following radiation therapy

Patient ID	Treatment	RECIST	Volume	Stiffness	Perfusion (K^{trans})	Pathology (N/V/F) (%)
12	Definitive RT	15%	13%	10%	10%	*
13	RT + S	15%	33%	49%	51%	40/29/31
14	RT + chemo + S	10%	12%	71%	47%	49/23/29
15	RT + S	8%	17%	4%	66%	12/83/6

Percent decrease from baseline in RECIST measurement, tumor volume, stiffness and perfusion. Abbreviations: RT = radiation therapy; S = surgery; chemo = chemotherapy; N = necrosis; V = viable; F = fibrosis.

* = patient did not have surgery but progressive disease was determined based on clinical findings.