

Changes in tumor stiffness post ⁹⁰Yttrium radioembolization therapy assessed with MR elastography: Early results.



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INTRODUCTION

⁹⁰Yttrium radioembolization (RE) is a locoregional therapy used as a bridge to transplantation in advanced disease cases or as a palliative tool in unresectable HCC. Microspheres containing ⁹⁰Yttrium are injected trans-arterially and travel to hepatic lesions due to preferential blood supply from the hepatic artery. Despite the well-established clinical benefit, RE side effects include hepatic dysfunction, edema and radiation related illness^{1,2}.

In this study we prospectively assess the effect of RE on the mechanical properties of the index lesion and the surrounding liver parenchyma by measuring tissue stiffness using MR elastography. MR elastography is a phase contrast technique which quantifies the stiffness of tissue by analyzing the propagation of externally induced shear waves through the organ of interest. There are currently no reports on the effect of RE on the index lesion and surrounding parenchyma stiffness following RE.

METHODS

In this preliminary IRB-approved single center study, MRE was performed on 13 prospectively enrolled cirrhotic patients (M/F 9/4, mean age 69.0±7.0 years) before and approximately 6 weeks after RE (12 segmental, 1 lobar) for HCC (mean interval between RE and post treatment MRI: 42.4±2.6 days).

MRE was performed at 1.5T (Aera, Siemens) over a single breath hold using an axial 2D SE-EPI sequence. Data were reconstructed inline by a commercially available inversion algorithm³ (Figure 2). The change in stiffness was assessed in the liver parenchyma remote to the treated lobe/segment, liver parenchyma in the treated lobe/segment and the index lesion itself. A radiologist assessed treatment response at 6w by calculating degree of tumor necrosis on subtracted post-contrast T₁ weighted VIBE images (after injection of gadoxetic acid, Eovist/Primovist, Bayer).

Stiffness changes following RE were tested for significance using Wilcoxon signed-rank tests. Mann-Whitney U tests were used to determine the significance of within-subject differences in parenchyma and lesion stiffness. Spearman correlations were determined between stiffness measurements and degree of tumor necrosis at 6w.

RESULTS

- Pre and post stiffness values for the measured tissues are displayed in **Table 1**
- Example pre and post RE images shown in **Figure 1**
- MRE unsuccessful in 3 patients, 10 HCCs (mean size 3.4±1.9 cm, range 1.5cm-8cm) were analyzed in 10 patients
- Tumor stiffness was significantly increased after RE (p=0.005; **Figure 2**), with mean increase of 56%
- Percentage change in tumor stiffness was significantly associated with degree of tumor necrosis at 6w post RE (r=0.665, p=0.036; **Figure 3**)
- Liver stiffness adjacent to treated lesion also significantly increased following therapy, (p=0.037; **Figure 4**)
- No difference was observed in liver stiffness away from the treated area after RE (p=0.21)

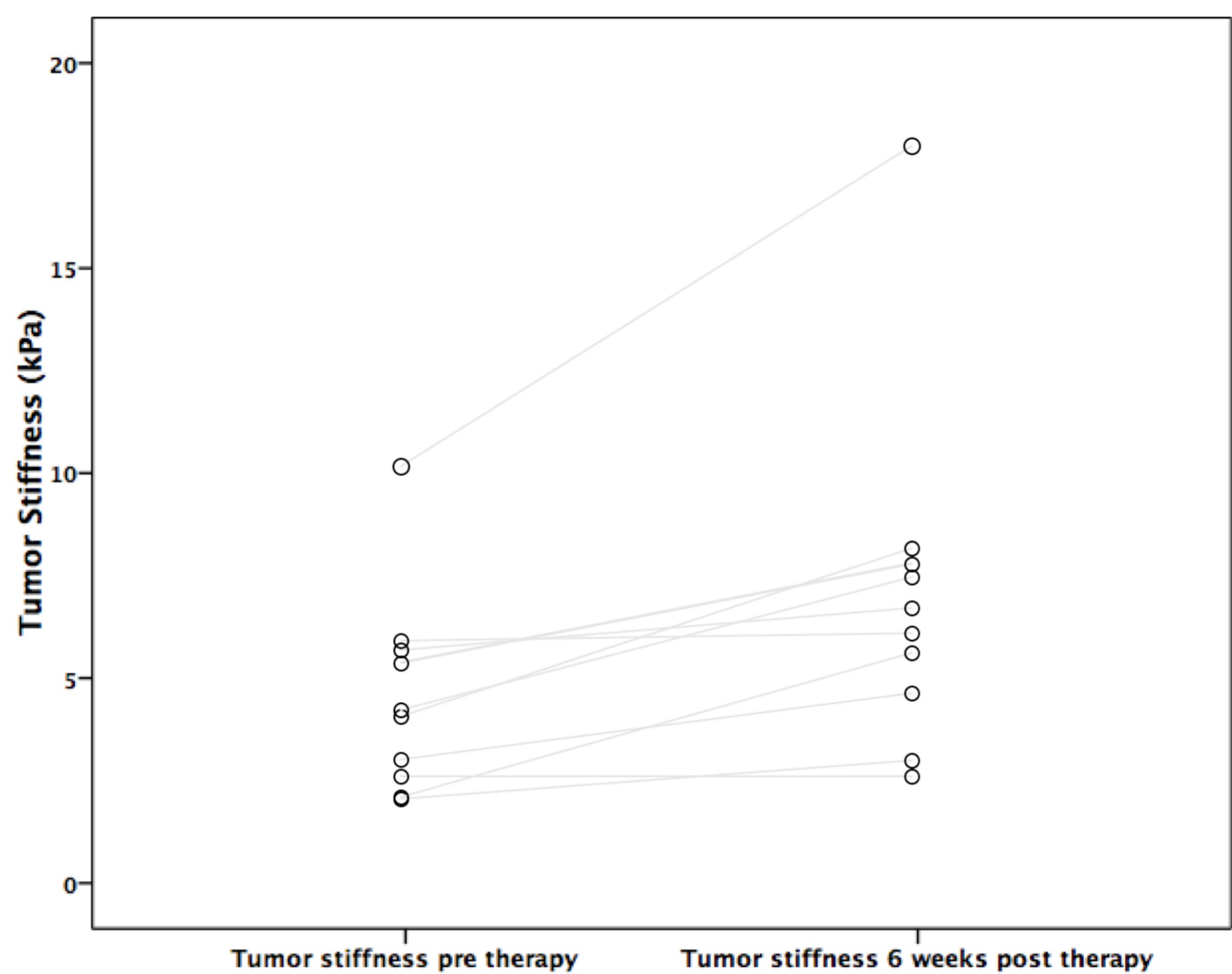


Figure 2. Linked plot displaying tumor stiffness before and 6w after RE therapy in 10 patients with 10 HCCs. 2/10 tumors showed stable stiffness (<5% increase), while the remaining 8 showed increased in stiffness (range 17-155%).

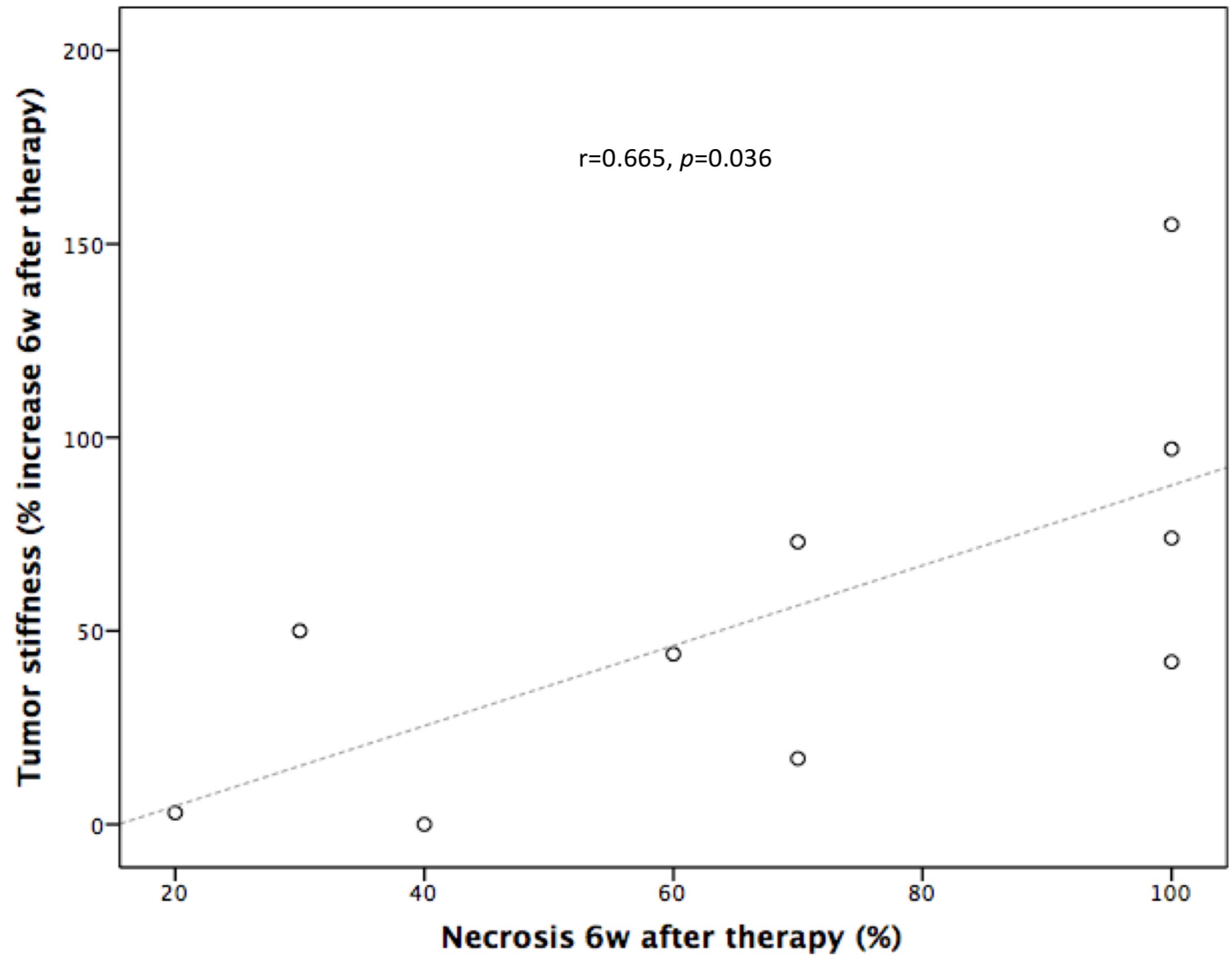


Figure 3. Scatter plot showing the relationship between percentage change in tumor stiffness and necrosis at 6w. A significant positive association is seen between the parameters.

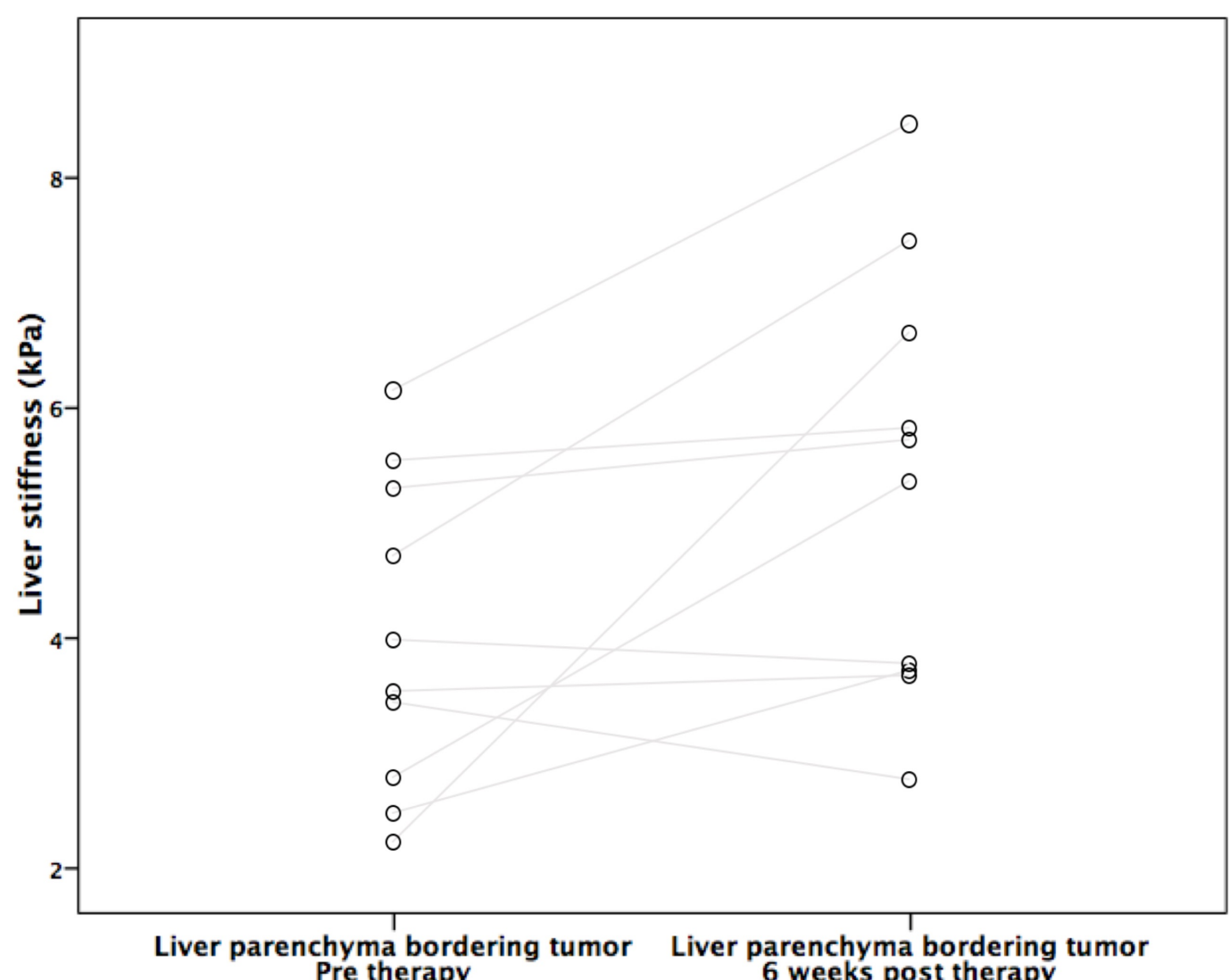


Figure 4. Linked plot displaying liver parenchyma stiffness adjacent to treated lesion before and 6w after RE therapy. Liver stiffness decreased in 2/10 patients, however in the remaining 8 there was an increase (range 4-199%).

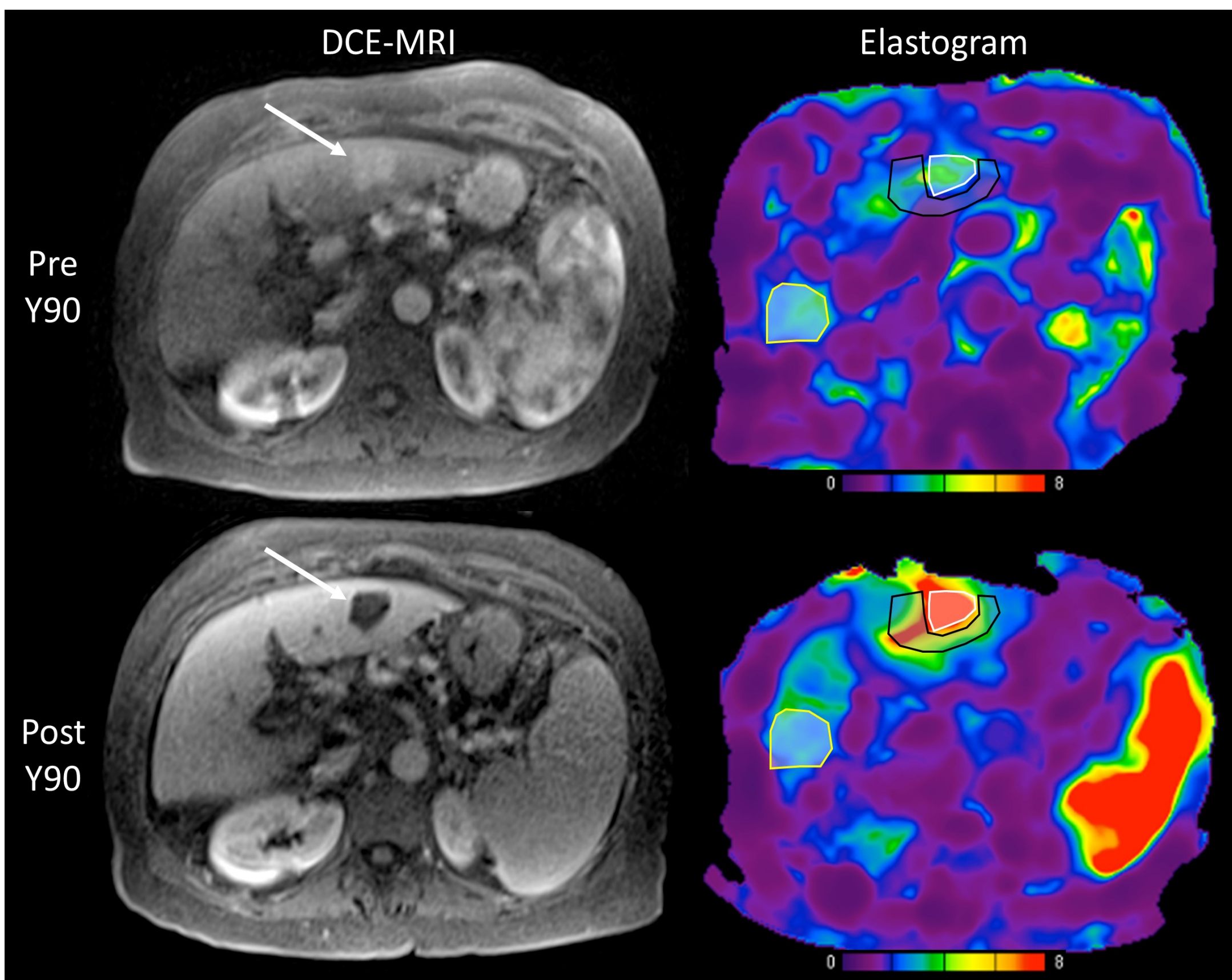


Figure 1: 76-year-old female patient with HCC pre (top) and 6w post RE (bottom). Top: DCE-MR images demonstrate arterial hyperenhancement (arrow), with tumor stiffness of 4.06 kPa. ROIs for tumor (white outline), adjacent liver tissue (black outline) and remote liver tissue (yellow outline) are illustrated. Bottom: DCE-MR image obtained during portal venous phase shows 100% necrotic lesion (arrow) with increased stiffness of 7.99 kPa. Similarly, liver stiffness adjacent to tumor increased from 2.25 kPa to 6.73 kPa.

Tissue	Pre (kPa)	Post (kPa)	Change (%)	p-value
Tumor	4.53±2.44	6.91±4.22	55.6±44.6	0.005
Liver – Adjacent to tumor	4.06±1.38	5.41±1.88	43.1±61.4	0.037
Liver – Distant to tumor	4.88±1.23	4.44±0.91	-3.4±14.1	0.21

Table 1. Mean±SD pre- and post RE stiffness values for HCC, liver parenchyma adjacent, and away from, the treated lobe/segment.

CONCLUSIONS

- These preliminary results suggest that HCC tumor stiffness and stiffness of surrounding liver increase at 6w after RE, and the percentage change in stiffness is significantly correlated with degree of tumor necrosis at 6w. pSWE produces a high proportion of unreliable measures
- A previous study reported a significant negative correlation between tumor stiffness post treatment and necrosis². In our study we also observed a negative correlation between tumor stiffness post treatment and degree of necrosis however it was not significant, potentially due to the small sample size. Also, the median interval between treatment and imaging was twice as long as that in our study (85 vs 42 days).
- The results indicate mechanical properties of tumor tissue and surrounding liver parenchyma change significantly early after RE therapy. The time course of stiffness change following therapy will be studied in a future larger study, including data on response to therapy at 6 months.

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