MyoMap quantification of myocardial toxicity following concurrent chemoradiotherapy for esophageal carcinoma

Simon Tang1,2,3; Eng-Siew Koh1,2,3; Robba Rai1,2,3; James Otton4; Mark Lee2,3; David Tran4; Lois Holloway1,2,3,5; Liza Thomas3,5; Benjamin Schmitt6; Gary Liney1,2,3

1. Ingham Institute of Applied Medical Research, Liverpool, NSW, Australia
2. Cancer Therapy Centre, Liverpool Hospital, NSW, Australia
3. University of New South Wales, NSW, Australia
4. Department of Cardiology, Liverpool Hospital, NSW, Australia
5. University of Sydney, NSW, Australia
6. Siemens Healthineers, Sydney, Australia

Introduction

Crude rates of symptomatic cardiac toxicity in esophageal carcinoma are reportedly 10.8% [1]. Cardiac manifestations including clinical findings such as pericardial effusion, arrhythmia, ischemia and cardiomyopathy, typically occur between 4 to 24 months following thoracic radiation [2, 3]. Subclinical manifestations including declines in mean ejection fraction [4] and perfusion abnormalities and wall ischemia [5] have also been noted at shorter time scales between 1–3 months. Hatakenaka et al. [6], using cardiac MRI, have demonstrated focal wall motion abnormalities in conjunction with changes in heart rate, stroke volume and left ventricular (LV) end-diastolic volume index following concurrent chemoradiation.

In-house quantification of longitudinal and cross sectional reproducibility in vivo has shown variation of 3.9% for T1 measurements, and a 15.2% variation in T2 measurements [7].

This paper presents the case of a patient treated with concurrent chemoradiation for esophageal cancer, where cardiac tissue properties were assessed by cardiac mapping (MyoMaps) longitudinally prior to, 6 weeks following, and 12 months following treatment.

Patient case

This 67-year-old male patient was diagnosed with a Stage IB T2N0M0 squamous cell carcinoma of the lower esophagus, following investigations for unexplained dysphagia and weight loss. He was otherwise fit and well, with the cardiac risk factors of hypercholesterolaemia and a smoking history.

T1 Relaxation: Measure of longitudinal signal recovery. This is elevated in the presence of edema or fibrosis.

T2 Relaxation: Measure of transverse signal decay. This is elevated in the presence of edema.

ECV: Is a measure of myocardial extracellular volume. It is elevated in myocardial fibrosis.

Table 1: Definitions.
He subsequently underwent chemoradiation 50 Gy / 25 fractions using a 3D conformal technique, with concurrent carboplatin/paclitaxel chemotherapy. He experienced no cardiac symptoms during or following his treatment.

**Image acquisition**

The patient underwent three separate cardiac MRI scans, one prior to, 6 weeks, and 12 months following completion of his chemoradiation. A clinical modified look locker inversion (MOLLI) sequence\(^1\) was used to generate myocardial short axis T1 maps (MyoMaps, Siemens Healthcare, Erlangen, Germany), pre- and 15 minutes post-administration of a gadolinium-based contrast agent, as well as T2 maps (MyoMaps) at 3 Tesla. T1, T1 post-contrast and T2 relaxation times of the LV were acquired with MRI mapping software (cv42, v4.5, Circle Software). Extracellular volume (ECV) was derived from the myocardial portioning coefficient (\(\lambda\)), adjusting for hematocrit. Values were recorded in the American Heart Association (AHA) 17 segment model \(^8\). Figure 1 illustrates the delineation of the left ventricle on a native T1 map. Definitions and possible significance of various MRI sequences are outlined in Table 1.

**Radiotherapy dose calculations**

Corresponding RT doses to the AHA LV segments were determined from contours outlined in the cardiac axes on reformatted planning CT images in Oncentra Brach Treatment Planning v4.5.2 (Elekta AB, Stockholm, Sweden), before being imported into Mim v6.77 (Mim Software, Beachwood, OH, USA) for dosimetric readout. Mean heart dose, mean LV dose, and mean segmental doses were reported, with mean heart doses having known associations with radiation induced cardiac toxicity \(^9\).

**Results**

The mean heart dose was 28.82 Gy. The mean LV dose was 14.16 Gy. Mean dose delivered to the left ventricular segments was heterogeneous, with segments 3 and 4 receiving 30 Gy or more, segments 2 and 5 receiving 20 Gy or more, and segments 6, 10, and 11 receiving 10 Gy or more. Figure 2 reports the dose delivered in a bulls-eye format.

Changes in the T1, T2, and ECV values are as illustrated in Figures 3–5, with the changes depicted on the MyoMaps represented in Figures 6 and 7. Visually there appears to be an increase in native T1 values post chemoradiation, most prominently 12 months following treatment, which is occurring most prominently in segments 3, 4, and 5, which correspondingly received the highest radiation doses. A 12 month increase in T2 relaxation time values was also seen, although occurring more globally throughout the left ventricle. The ECV percentage transiently increased 6 weeks following chemoradiation.

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\(^1\) WIP, the product is currently under development and is not for sale in the US and in other countries. Its future availability cannot be ensured.

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*Figure 2: Dose delivered to the left ventricular segments represented in a bulls-eye format.*

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**Left ventricular segmentation**

- 1. basal anterior
- 2. basal anteroseptal
- 3. basal inferoseptal
- 4. basal inferior
- 5. basal inferolateral
- 6. basal anterolateral
- 7. mid anterior
- 8. mid anteroseptal
- 9. mid inferoseptal
- 10. mid inferior
- 11. mid inferolateral
- 12. mid anterolateral
- 13. apical anterior
- 14. apical septal
- 15. apical inferior
- 16. apical lateral
- 17. apex

**Dose delivered (Gy)**

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*siemens.com/magnetom-world-rt*
Figure 3: T1 values

(3A) Pre-treatment
(3B) 6 week post-treatment
(3C) 12 months post treatment time points respectively

Elevation of T1 values were most pronounced at 12 months in the basal segments.

Figure 4: T2 values

(4A) Pre-treatment
(4B) 6 week post-treatment
(4C) 12 months post treatment time points respectively

Elevation of the segments 7, 11, 12, 13, and 16 in 4A are artefactual from errors in motion correction. An increase in T2 values in predominantly the basal segments was seen after 12 months.
Figure 5: ECV values

(5A) Pre-treatment
(5B) 6 week post-treatment
(5C) 12 months post treatment time points respectively

A subtle increase in ECV is seen the basal segments following treatment, however returns to baseline at 12 months.

Figure 6: Basal slice through left ventricle – T1 maps

(6A) MyoMaps through the basal segments pre-treatment, individual segments being labelled from one to six
(6B) 6 weeks post
(6C) 12 months post treatment respectively

A qualitative change (increase in relaxation time) can be seen affecting the myocardium in segments 3, 4, 5, and 6 which may indicate myocardial inflammation or fibrosis.
Conclusion

The use of MyoMaps for quantitative assessment of the myocardium following cancer therapy treatment shows promise, and experience with this patient has demonstrated feasibility. In this single case study, there was an elevation of T1 and T2 relaxation times occurring 12 months following treatment, which is preceded by an increase in ECV percentage immediately following chemoradiation. These results must be placed in the context of inherent variability in T1/T2 measurements. Further studies will be required in order to determine if the findings reported in this case are significant.

The use of cardiac MRI mapping however may provide novel information regarding acute to sub-acute myocardial changes following radiation therapy.

Contact

Associate Professor Gary Liney (UNSW)
Hon. Principal Fellow, University of Wollongong Ingham Institute for Applied Medical Research & Radiation Oncology
Liverpool Hospital
1 Campbell Street
Liverpool NSW 2170
Australia
Tel.: +61 2 8738 9221
gary.liney@sswhs.nsw.gov.au

References