Ultra-sound Shear Wave Elastography Tissue Stiffness and Thickness Assessment After Adjuvant Radiotherapy for Breast Cancer Treatment; An Exploratory Study.

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Research Article

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Abstract

Purpose: This research investigated the feasibility of using B-mode ultrasound with shear-wave elastography (SWE) to evaluate the structural and mechanical properties of multiple tissue layers in the pectoral region of women with chronic radiation fibrosis following breast cancer treatment.

Method: Nine women between one and five years post unilateral conventional fractionated radiotherapy were evaluated. Both ultrasound and SWE were used to examine the thickness and stiffness of skin, subcutaneous adipose tissue, fascia and muscle in both their irradiated and non-irradiated sides.

Linear mixed models were conducted to examine statistical differences in tissue thickness and stiffness between irradiated and non-irradiated sides with the arm resting by the side and also in abduction.

Results: Significant differences were found between irradiated and non-irradiated tissues. Irradiated skin was significantly thicker ($p=0.020$) and stiffer ($p<0.001$) with the arm by the side. Irradiated subcutaneous adipose tissue was significantly thinner ($p<0.001$). Irradiated fascia and muscles thinned significantly with the arm moved out to abduction position. Irradiated pectoral muscle was significantly stiffer ($p=0.004$), this stiffness amplified with arm abduction ($p<0.001$) where the muscle thinned significantly ($P<0.001$).

Conclusion: Ultrasound with SWE shows potential to provide novel objective evaluation of radiation induced soft tissue fibrosis at multiple tissue layers in the pectoral region. Tissue thickness changes in irradiated tissue were evident in ultrasound images. Quantifying these tissue changes supports research development and introduction of clinical interventions to ameliorate the symptoms of morbidity that is currently considered irreversible.

Introduction

Radiation fibrosis describes chronic tissue changes that occur in multiple tissues following the use of radiotherapy for the treatment of cancer. Ionizing radiation used to irreparably damage cancer cells also damages surrounding healthy tissues generating thickened, stiff, contracted and adhered layers of skin, fascia and muscle [1]. Radiation fibrosis can present as a progressive disorder with ongoing tissue contraction over a patient’s lifetime [2–6]. It occurs in approximately 30% of breast cancer patients [3] limiting movement and reducing quality of life [4, 7–11]. Currently there is no curative treatment with evidence of ongoing efficacy. Anecdotal evidence from clinical reports suggest early diagnosis and therapy may reduce long term functional morbidity [1, 5, 11, 12]. Research to develop effective therapies has been hindered by lack of assessment tools to objectively evaluate changes in the structural and mechanical properties of affected tissues [5]. The extent (depth and degree) of bio-physical damage to an individual’s therapeutically irradiated tissues is currently difficult to assess, and the long-term functional repair of individual tissues after radiotherapy is unknown. This information is vital for accurate assessment and to target and optimize therapies to improve functional outcomes for patients.

Ultrasound (US) with Shear Wave Elastography (SWE) is emerging as a potential tool to evaluate the structural and mechanical properties of individual tissues at multiple tissue depths. It uses non-ionising imaging technology capable of providing objective measurements of skin [13–15], adipose tissue [16, 17], fascia [18] and muscle [10, 16, 19] thickness and stiffness. If suitable, this technology has the potential to diagnose stage and evaluate the progression of the radiation fibrosis to enable early detection, individualise patient treatment and to evaluate the efficacy of both current and novel treatments. The aim of this study was to explore the feasibility of using SWE to evaluate the skin, subcutaneous adipose tissue, fascia and pectoral muscle in women with chronic radiation fibrosis following treatment for breast cancer. The elements evaluated were 1) whether US and SWE were sensitive enough to detect differences in thickness and stiffness at individual tissue levels, 2) whether a gel stand-off pad was required to evaluate the skin, 3) if the position of the arm influenced measurements and 4) the clinical time burden to evaluate multiple tissue levels in two different arm positions. This feasibility study will support funding applications regarding use of ultrasound and elastography in randomised trial exploring early interventions to ameliorate effects of radiation fibrosis.

Materials And Methods

This was a single centre feasibility study with institutional ethics approval of the protocol 8/10/2019 (RGS 0000003365). Written informed consent was obtained from all subjects in accordance with the World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects as required for approval of the Western Australian Health Ethics application, via the Research Governance Ethics Executive Officer of the Sir Charles Gairdner Osbourne Park Health Care Group.

A convenience sample was selected due to limited access to the imaging system. Women who had received physiotherapy treatment for radiation fibrosis were recruited from the Sir Charles Gairdner Hospital Breast Centre. Participants were over 18 years of age, had surgical mastectomy and adjuvant unilateral chest wall conventional fractionated radiation treatment. In our institution routine mastectomy retains the pectoral fascia. Exclusion criteria included women with bilateral chest radiation therapy, Systemic Lupus Erythematosus, or connective tissue or skin conditions such as dermatitis, eczema, or psoriasis. Pregnant or lactating women or those unable to provide informed consent due psychological, cognitive or language barriers were also excluded. Patients currently undergoing chemotherapy or treatment for current breast cancer were excluded.

An ACUSON Sequoia ultrasound system was used for all examinations (Siemens Healthineers Pty Ltd Australia and New Zealand). Brightness (B) -mode US imaging was used to measure tissue thickness using an 18L6HD transducer and SWE was obtained using a 10L4 transducer to measure tissue stiffness within the selected Region of Interest (ROI).

Procedure:

Participants were first examined lying supine with the arm supported by the side to image the pectoralis major muscle, then with the arm supported in 90^0 abduction so the pectoralis major muscle fibres were in a more lengthened state.

A single sonographer (SH) evaluated all participants. The ROI was selected above the surgical site, within the irradiated treatment field over the clavicular portion of pectoralis major muscle, inferior to the clavi-pectoral triangle and medial to the delto-pectoral groove. A contralateral non-irradiated matched location was subsequently imaged as the control.

A thick layer of transmission gel was placed on the skin then the 18L6HD transducer was placed perpendicular to the chest wall and the muscle fibres [20], taking care not to apply pressure. A B-mode image was acquired ensuring a clear entry echo was visible, then using the calliper function five equidistant measurements of tissue thickness were taken at each tissue layer (skin, subcutaneous adipose, fascia and muscle). Transmission gel was reapplied if necessary and the 10L4 transduced was placed in the same location. The system was switched to SWE mode and an image acquired. The image was evaluated for quality and repeated if necessary. Five equidistant sampling boxes ($1.5mm^2$) were placed within each tissue layer to obtain the shear wave velocity (SWV) recorded in metres per second (m/s). The mean of these five measurements was recorded for each tissue layer. The process was repeated on the contralateral side, then repeated bilaterally with the arm in abduction. Additionally, extra SWE images were acquired of the skin using the same protocol and a previously developed custom 'gel-well' stand-off [21]. The 'gel-well' is a rectangular silicon structure with a central cut-out designed to contain transmission gel so that a standard thickness of 10mm gel is maintained. All images were evaluated independently by a radiologist (AB), blinded to the treatment side, to confirm the target area had been captured and report any subjective findings.

Statistics:

Data were analysed using Stata 16.0 (StataCorp LLC, College Station, Texas). Descriptive statistics were based on frequency distributions for categorical data and medians, IQRs, and ranges for continuous data.

The mean thickness and SWV for each tissue layer were calculated and used for further analysis. Linear mixed models were conducted to examine differences in outcomes (tissue thickness, SWV) between irradiated and non-irradiated sides with the arm at rest by the side and also in abduction. Results were summarised as estimated means and corresponding 95% confidence intervals (CIs). *P* values <0.05 were considered statistically significant. A post power calculation indicated a sample of n=9 has 80% power to detect a standardised mean difference (effect size dz) of 1.07 in correlated data points or matched pairs (two-tailed, alpha=0.05). (G*Power 3.1.9.2).

Correlation between the stiffness and thickness of each tissue layer was evaluated using Spearman's correlation coefficients. Spearman r values between 0.9 and 1 (-0.9 to -1) indicate a very high correlation, those from 0.7 to 0.9 (-0.7 to -0.9) a high correlation, those from 0.5 to 0.7 (-0.5 to -0.7) a moderate correlation and those below 0.5 (above -0.5) a low correlation (Mukaka 2012) [22].

Results

Ten women were recruited to the study; however, one was unable to attend, resulting in nine participants. Demographic information and treatment details of the participants are presented in Table 1. The radiation fields of all participants' included chest wall, supraclavicular fossa and lower axillary lymph nodes with four participants additionally having axillary field included. Participants were between one and five years (median 1.5, IQR 1.1, 2.2: min 0.6, max 4.2) post radiation treatment for breast cancer. All participants had recently completed physiotherapy treatment for post radiotherapy onset tissue stiffness with associated discomfort and loss of arm range of motion. On the day of US imaging participants' tissue stiffness was reported as not manually palpable by the team members present.

Table 1
Participant Demographics and Treatment Details.

Participant (n=9)	**Age *median (IRQ)***
at radiotherapy start	58.8 (10.2)
BMI at surgery *mean (SD) [min-max]*	29.8 (5.8) [18.0 – 37.5]
BMI category *Number (%)*	
Underweight (<18.5)	1 (11.1)
Normal	-
Overweight (25-29.9)	2 (22.2)
Obese (≥30)	6 (66.7)
Smoking Status *Number (%)*	
Never	4 (44.4)
Current	1 (11.1)
Ex	3 (33.3)
Surgery (n=9)	*Number (%)*
Tumour laterality	
Right	6 (66.7)
Left	3 (33.3)
Mastectomy	
Unilateral	6 (66.7)
Bilateral	3 (33.3)
Sentinel Lymph Node Biopsy (SLNB)	
Unilateral	1 (11.1)
Bilateral	3 (33.3)
Axillary Lymph Node Resection (ALNR)	
Unilateral	8 (88.9)
Bilateral	-
Surgery complications	
All	5 (55.6)
Infection	1 (11.1)

Participant (n=9)	**Age *median (IRQ)***
Seroma	5 (55.6)
Radiotherapy Treatment Field (n=9)	*Number (%)*
Chest wall	9 (100.0)
Supraclavicular fossa	9 (100.0)
Axilla	4 (44.4)
RT duration (days) *med (IQR) [min-max]*	35 (35, 36) [32-36]
RT Dose	
Grays (Gy) administered	50 *(all)*
Fractionation schedule (fractions)	25 *(all)*
Other Treatments (n=9)	*Number (%)*
Hormone therapy	5 (55.6)
Adjuvant Chemotherapy	4 (44.4)
Swelling *Number (%)*	
In imaging Region of Interest	4 (44.4)
Near imaging Region of Interest	7 (77.8)
Range of Motion at abduction *med (IQR) [min-max]*	95 (90, 108) [90-135]

Linear Mixed Models

The estimated means of tissue thickness and SWV are summarised in Tables 2 and 3 respectively. Visual representation of these results can be seen in Figures 1, 2 and 3.

Table 2
Estimated (Est.) mean tissue thickness in millimetres using B-mode Ultrasound.

N=9	**Control side**	**Treatment side**	
Arm at rest	**Est. Mean (95%CI)**	**Est. Mean (95%CI)**	**p-value**
Pectoral skin	1.36 (1.07-1.65)	1.42 (1.14-1.71)	0.020
Subcutaneous tissue	11.91 (10.22-13.59)	8.32 (6.63-10.01)	<0.001
Pectoral fascia	0.55 (0.48-0.63)	0.53 (0.46-0.61)	0.425
Pectoral muscle	9.95 (9.04-10.85)	10.12 (9.21-11.03)	0.542
All combined	5.94 (5.35-6.53)	5.02 (4.42-5.62)	0.016
Arm at 90° abduction			
Pectoral skin	1.45 (1.15-1.75)	1.50 (1.20-1.81)	0.049
Subcutaneous tissue	13.00 (10.73-15.27)	9.91 (7.64-12.18)	<0.001
Pectoral fascia	0.58 (0.51-0.64)	0.49 (0.42-0.55)	<0.001
Pectoral muscle	10.95 (10.14-11.76)	10.00 (9.19-10.80)	<0.001
All combined	6.49 (5.78-7.21)	5.47 (4.76-6.19)	<0.001

CI: (confidence interval).

Table 3
Estimated (Est.) mean Shear Wave Velocity (metres/second) comparing control side with radiotherapy treated side. No stand-off pad used.

	Control side	**Treatment side**	
	Est. Mean (95%CI)	**Est. Mean (95%CI)**	p
Arm at rest			
Pectoral skin	1.47 (1.32-1.62)	1.63 (1.47-1.78)	0.009
Subcutaneous tissue	1.14 (0.95-1.33)	1.21 (1.02-1.40)	0.309
Pectoral fascia	2.36 (2.16-2.56)	2.13 (1.93-2.33)	0.079
Pectoral muscle	1.69 (1.45-1.93)	1.99 (1.75-2.23)	0.004
All combined	1.68 (1.56-1.80)	1.75 (1.63-1.87)	0.314
Arm in 90° abduction			
Pectoral skin	1.68 (1.46-1.90)	1.67 (1.45-1.89)	0.887
Subcutaneous tissue	1.04 (0.84-1.24)	0.94 (0.74-1.14)	0.389
Pectoral fascia	2.56 (2.19-2.94)	2.86 (2.48-3.23)	0.085
Pectoral muscle	1.68 (1.46-1.90)	1.67 (1.45-1.89)	0.887
All combined	1.81 (1.63-1.98)	2.03 (1.86-2.21)	0.003
CI: confidence interval			

With the arm resting by the side, the mean skin thickness was significantly higher on the irradiated side compared to the control side whereas the mean thickness of the irradiated subcutaneous tissue was significantly thinner than the control. No statistically significant differences in mean thicknesses were noted in the fascia or pectoral muscle. Overall, the mean combined tissue thickness on the irradiated side was significantly thinner compared to the control side.

The SWV was significantly higher (stiffer) in both the irradiated skin and muscle compared to the controls with the arm by the side. This is represented in Figure 2. However, neither the subcutaneous adipose or fascia were significantly different to the control side, neither was the stiffness of all tissues combined.

With the arm abducted to 90^{o} the mean thickness was significantly different between all irradiated tissue layers compared to controls. This is represented in Figure 1. The skin was significantly thicker on the irradiated side, however the subcutaneous tissue, fascia and pectoral muscle on the irradiated side was significantly thinner than the control side. The overall thickness of irradiated tissues was significantly thinner than the control when the arm was at 90^{0} abduction.

The SWV of irradiated muscle was the only tissue layer that was significantly stiffer than the control side in 90^0 arm abduction, with no significant differences in the stiffness of the other tissue layers. Figure 3 represents this. The overall stiffness of all tissues layers combined was significantly stiffer than the controls.

Significant differences in stiffness between the arm by side and arm abducted positions were noted (Table 4). The healthy skin (control side) was the only tissue layer significantly stiffer in abduction compared to arm by side position. The irradiated (treatment side) fascia and muscle were both significantly stiffer in abduction compared to arm by side. The irradiated subcutaneous tissue shear wave speed significantly decreased in the abduction position. The thickness of the control side pectoralis major muscle was significantly increased in abduction compared to the arm by side position but the thickness did not change significantly on the treatment side.

Table 4

Comparison of estimated (Est.) mean Shear Wave Velocity (metres/second) between the arm resting by the side and in the abducted positions. Use of the stand-off “gel-well” compared to not using the stand-off technique is recorded for the skin alone, due to the possible benefit for measurement accuracy in skin. Below this comparison of SWV between arm at rest by the side and arm abducted positions in each tissue layer is displayed, being measured without a stand-off.

	Control side			**Treatment side**		
	Rest	**Abduction**		**Rest**	**Abduction**	
	Est. Mean (95%CI)	**Est. Mean (95%CI)**	**p-value**	**Est. Mean (95%CI)**	**Est. Mean (95%CI)**	**p-value**
Stand-Off						
Pectoral skin	1.60 (1.46-1.74)	1.87 (1.65-2.09)	<0.001	1.77 (1.63-1.91)	1.75 (1.53-1.97)	0.758
No Stand-Off						
Pectoral skin	1.47 (1.32-1.62)	1.68 (1.46-1.90)	0.004	1.63 (1.47-1.78)	1.67 (1.45-1.89)	0.825
Subcutaneous tissue	1.14 (0.95-1.33)	1.04 (0.84-1.24)	0.317	1.21 (1.02-1.40)	0.94 (0.74-1.14)	0.008
Pectoral fascia	2.36 (2.16-2.56)	2.56 (2.19-2.94)	0.204	2.13 (1.93-2.33)	2.86 (2.48-3.23)	<0.001
Pectoral muscle	1.69 (1.45-1.93)	1.81 (1.40-2.22)	0.284	1.99 (1.75-2.23)	2.52 (2.12-2.92)	<0.001
CI: (confidence interval)						

Stand-off vs no stand-off in skin

Significant differences in the SWV in skin were noted if a stand-off was used in the arm by side and abducted position for control tissue, but this was only significantly different in the treatment side in the arm by side position (Table 5). However, the relationships (significant differences) between irradiated and non-irradiated sides were similar regardless of the use of stand-off, suggesting the accuracy of measurements were compromised but not the relative measurements.

Table 5
Differences in estimated (Est.) mean Shear Wave Velocity (metres/second) when evaluating skin with or without a stand-off.

	No Stand-Off (NSO)			Stand-Off (SO)			Difference	
	Control	Treatment		Control	Treatment		Cont-rol	Treat-ment
	Est.Mean (95%CI)	Est.Mean (95%CI)	p	Est.Mean (95%CI)	Est.Mean (95%CI)	p	p	p
At rest	1.47 (1.32-1.62)	1.63 (1.47-1.78)	0.009	1.60 (1.46-1.74)	1.77 (1.63-1.91)	<0.001	0.023	0.007
Abducted	1.68 (1.46-1.90)	1.67 (1.45-1.89)	0.887	1.60 (1.46-1.74)	1.77 (1.63-1.91)	<0.001	0.012	0.250
CI: (confidence interval)								

Spearman’s Correlation Coefficient

Table 6 shows moderate correlations between the stiffness and thickness of both subcutaneous adipose tissue and muscle on the Treatment side with the arm resting by the side. A negative correlation is seen in the adipose tissue whereas the fascia had a positive correlation. Low correlations can be seen in all the healthy tissues and the skin and muscle of irradiated tissue.

Table 6
Spearman's Correlation coefficients demonstrating the correlation between the thickness and stiffness of each tissue layer with the arm resting by the side.

	Control side Rho	Treatment side Rho
Pectoral skin	0.077	0.105
Subcutaneous tissue	-0.312*	-0.571***
Pectoral fascia	-0.054	0.566***
Pectoral muscle	-0.384**	0.054
*p<0.05; **p<0.01, ***p<0.00		

The time taken to image and measure the thickness and stiffness of the skin, subcutaneous adipose, fascia and muscle on both sides of the body, in both neutral and abducted positions was approximately

45 minutes per patient.

Discussion

This feasibility study was designed to determine if both ultrasound and SWE were capable of quantifying differences between the thickness and stiffness of irradiated and non-irradiated tissues to detect radiation fibrosis. Although this study was small and consisted of participants with clinically non-palpable fibrosis at the time of assessment, differences between the irradiated and non-irradiated tissues were statistically significant at multiple tissue levels. This demonstrates that these forms of imaging have potential to identify subclinical differences in the tissues' structural and mechanical properties which is useful for early identification of fibrosis and to evaluate treatment efficacy.

The tissues in this study were evaluated in both an arm resting by the side position and in 90^0 abducted position to evaluate if tissue changes were more prominent in either position. In arm abduction, the healthy control side skin was the only control side tissue layer to significantly stiffen, whereas the subcutaneous adipose tissue, fascia and muscle were significantly stiffer in irradiated tissues. Larger studies including participants with varied degrees of fibrosis are required, however these results indicate value in researching the effect of radiation fibrosis on individual tissues. Insight to the long term structural and mechanical impact of radiotherapy on tissues in different postural positions furthers understanding the functional morbidity associated with radiation fibrosis. In this study, residual tissue stiffness suggests fibrotic changes persist despite persistent manual deep tissue release treatments and arm movement recovery. Future studies using SWE could evaluate the relationship between fibrotic changes and functional morbidity as continued therapy may be required for these individuals to maintain functional improvement due to the insidious contractile nature of radiation fibrosis.

The results of this study suggest variation in the response to radiation therapy within individual soft tissues. The irradiated skin was thicker than the control in both neutral and abducted positions. This is consistent with epidermal thickening described post radiation therapy [23] while the thinner subcutaneous adipose tissue finding is consistent with a previous study of post irradiation neck fibrosis [24]. Additionally, our study suggested that both the irradiated skin (arm at rest) and muscle (in both positions) were significantly stiffer than controls, but the subcutaneous adipose or fascia tissues were not. Objective assessment with ultrasound elastography could improve understanding of post radiation tissue morbidity, the effect on function, and enhance targeting therapies to specific tissues which could improve post treatment quality of life.

Using a stand-off for evaluating the skin resulted in higher SWV compared to no stand-off, however the significant relationships between irradiated and healthy skin remained the same regardless of whether a stand-off was used. These results support the notion that the distance between the probe and skin influences the accuracy of the measurement, however, it refutes the idea that there is an increased risk of compression artefact without the thicker layer of transmission gel [13]. The optimal stand-off thickness to optimise measurement accuracy for the skin is not yet determined.

Subcutaneous adipose tissue stiffness and thickness demonstrated a moderate negative correlation suggesting that thinner adipose was stiffer which is consistent with previous research following radiation treatment of head and neck cancer [24]. Adipose fibrosis contributes to long term metabolic dysfunction [17, 25] associated with cancer [26]. Fascia on the other hand demonstrated a moderate positive correlation between thickness and stiffness, which is consistent with reduced movement of fascia. Further research is required to evaluate the relationship between tissue stiffness and thickness change to understand the bio-physical interactions induced during radiation fibrosis and to identify the optimal time for therapeutic interventions for different tissues.

The study evaluation process took approximately 45 minutes, which is a lengthy assessment. However, we perceive the information value justifies the assessment.

Conclusion

This feasibility study demonstrated that US with SWE does provide objective measurement of the structural and mechanical properties of multiple pectoral tissue layers. Although the assessment protocol in this study was lengthy, it provides valuable insight into soft tissues affected by radiation fibrosis. This has relevance to timely diagnosis, functional morbidity and potentially both pharmaceutic and rehabilitation treatment efficacy. Further studies are recommended to facilitate earlier diagnosis, monitoring progression and evaluating efficacy of protective strategies and treatment radiation fibrosis.

Declarations

AUTHORS CONTRIBUTION: All authors contributed to the research.

Study concept: Catherine Hunt, Anita Bourke, Joshua Dass, Tammy Corica, Sueli Hardwick, Helen DeJong.

Study design: Catherine Hunt, Anita Bourke, Joshua Dass, Tammy Corica, Sueli Hardwick, Helen DeJong, Angela Jacques.

Material Preparation and data collection: Catherine Hunt, Anita Bourke, Joshua Dass, Tammy Corica, Sueli Hardwick, Helen DeJong.

Data preparation and analysis: Catherine Hunt, Anita Bourke, Joshua Dass, Tammy Corica, Sueli Hardwick, Helen DeJong, Greta Busch.

First draft written by: Catherine Hunt, Anita Bourke, Helen DeJong.

All authors commented on the final version, and approved it for submission.

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CONFLICT OF INTEREST:

The authors declare no conflict of interest and have no industrial affiliation.

Siemen's Healthineers ACUSON Sequoia ultrasound system was used for all examinations, however Siemen's Healthineers have not been involved in research design, data collection, data analysis or data interpretation, nor have they had the opportunity to discuss, view or comment on this manuscript.

ETHICS APPROVAL: Was obtained in accordance with the World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects as required for approval of the Western Australian Health Ethics application, via the Research Governance Ethics Executive Officer of the Sir Charles Gairdner Osbourne Park Health Care 8/10/2019 (RGS 0000003365).

CONSENT TO PARTICIPATE AND PUBLISH: Written informed consent to participate in the research and for publication was freely given by all subjects.

AVAILABILTY OF DATA: Data were analysed using Stata 16.0 (StataCorp LLC, College Station, Texas). The datasets used for the study are available from the authors on request.

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Figures

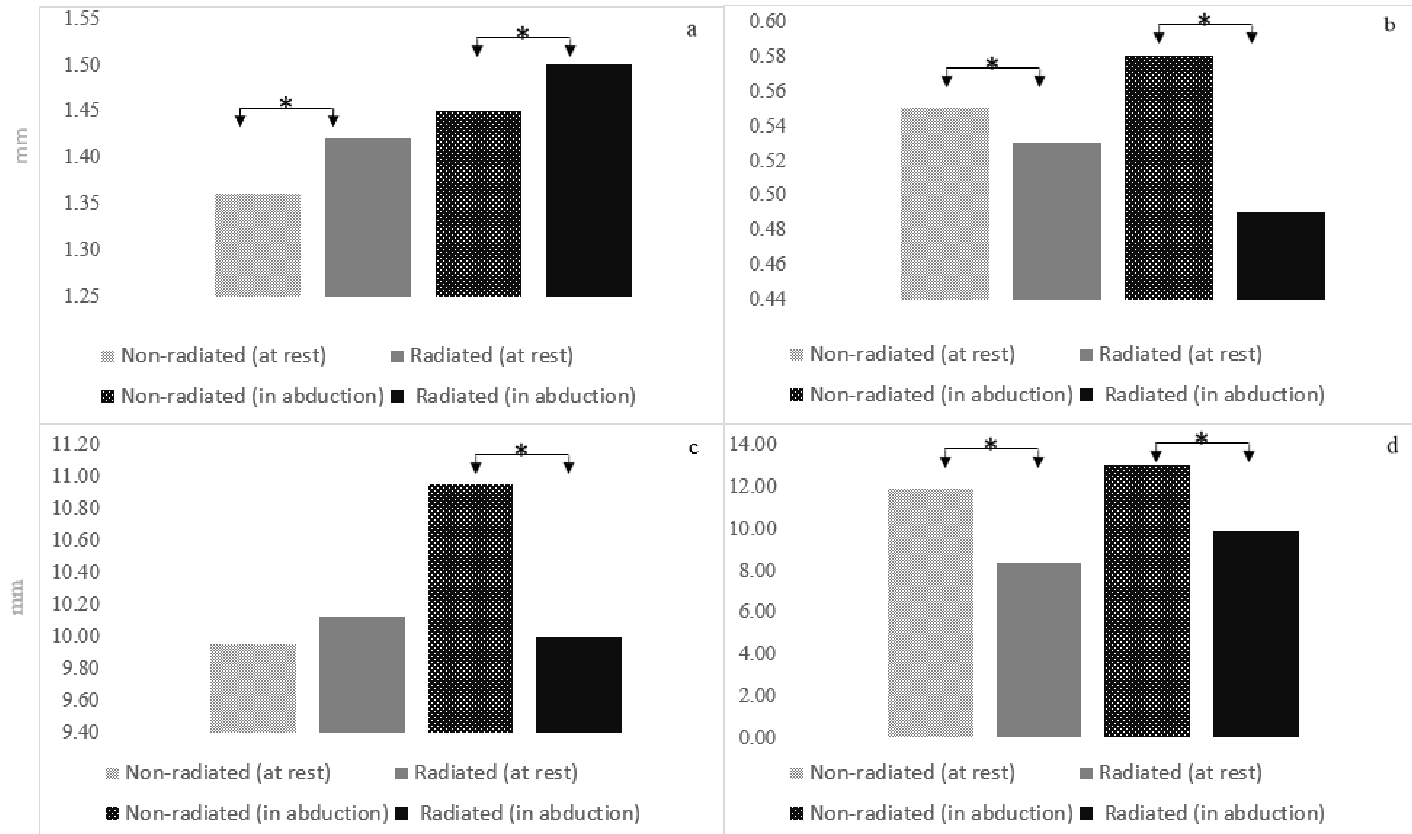
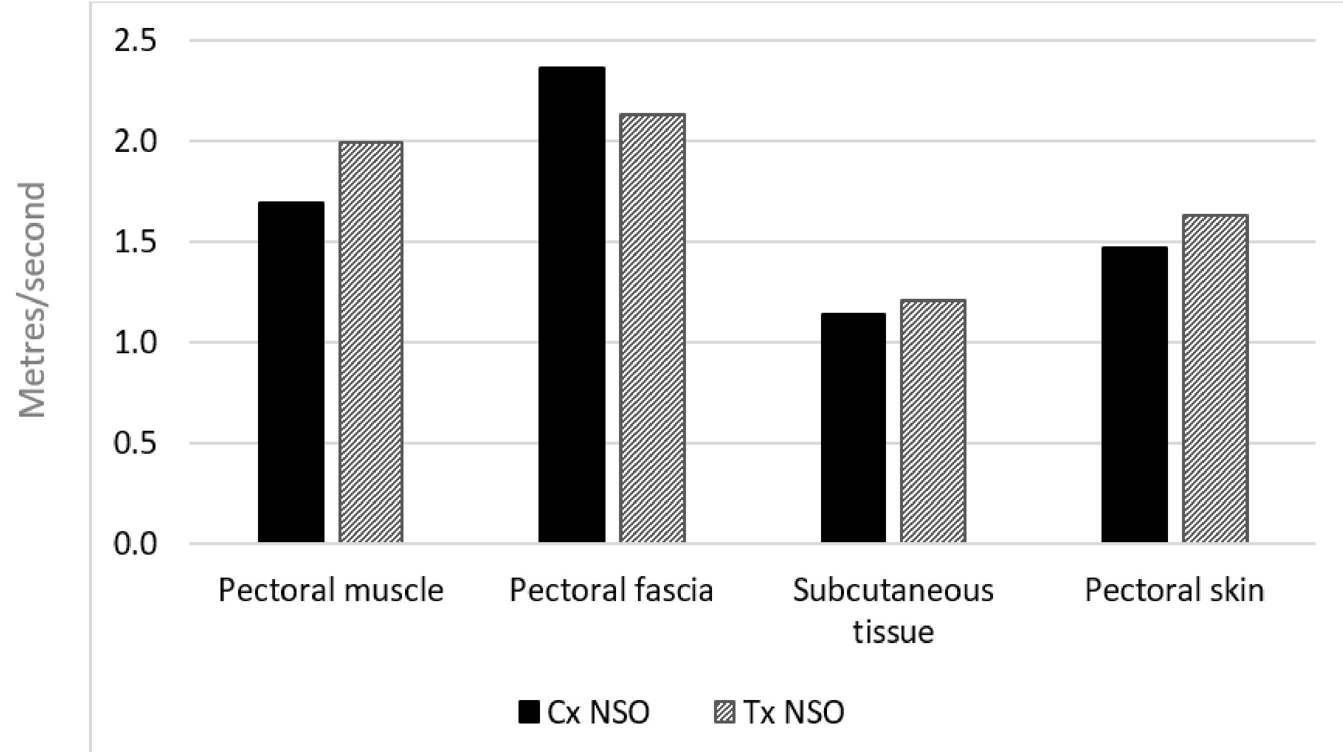


Figure 1

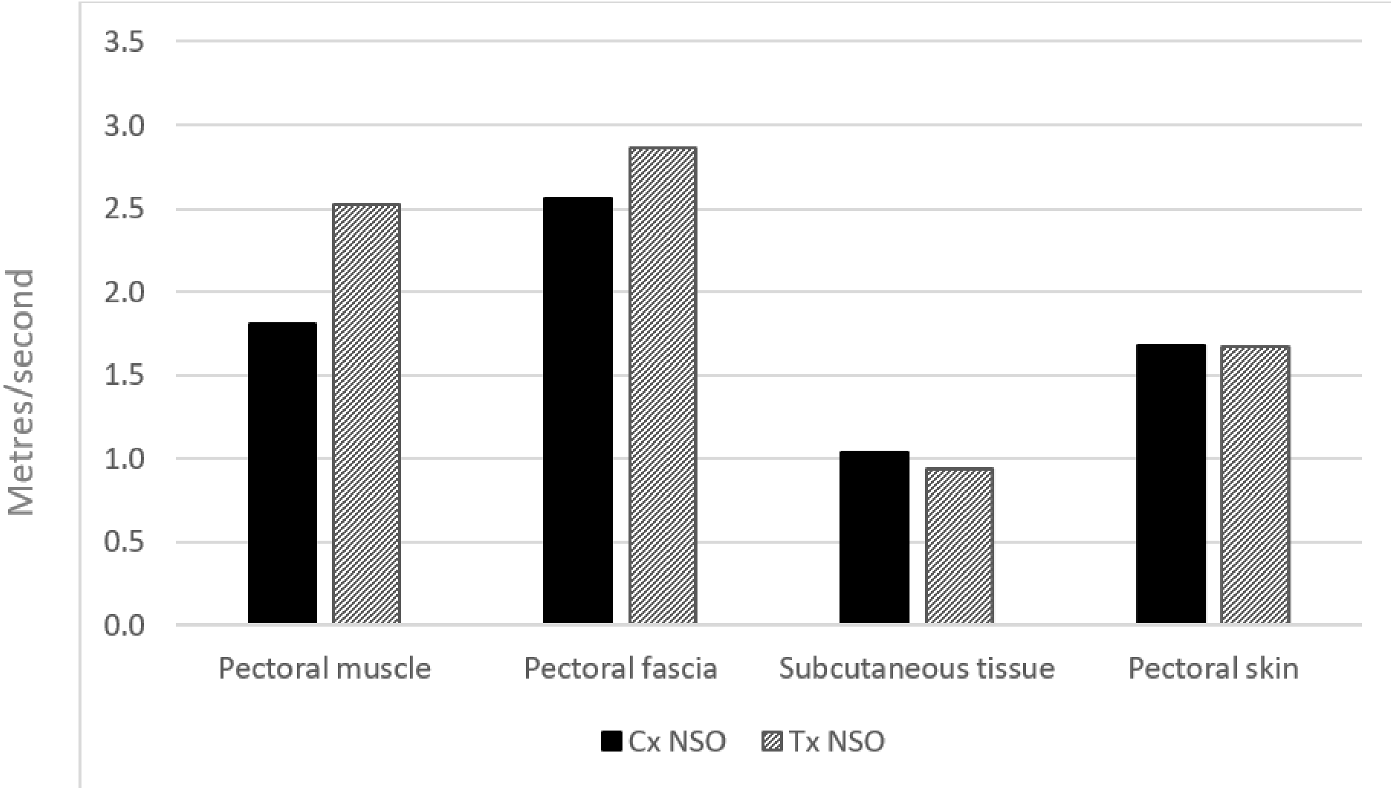
Estimated mean tissue thickness in millimetres (mm) using B-mode Ultrasound in Pectoral skin (a), pectoral fascia (b), Pectoral muscle (c) and Pectoral Subcutaneous tissue (d). An asterisk (*) indicates p<0.05.



Cx (Control side), Tx (Treatment side), NSO (No Stand Off).

Figure 2

Comparison of estimated mean shear wave velocity (metres/second) between control (Cx) and radiotherapy treated (Tx) Pectoral muscle, Pectoral fascia, Subcutaneous tissue and Pectoral skin tissues taken without the silicone stand-off pad (NSO) with the arm at rest by the side.



Cx (Control side), Tx (Treatment side), NSO (No Stand Off).

Figure 3

Comparison of estimated mean shear wave velocity (metres/second) of control (Cx) and radiotherapy treated (Tx) Pectoral muscle, Pectoral fascia, Subcutaneous tissue and Pectoral skin tissues taken without a silicone stand-off pad (NSO) with the arm at 90° abduction