

ORIGINAL ARTICLE

Shoulder morbidity after treatment for breast cancer is bilateral and greater after mastectomy

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Abstract

Background. A recent study in our laboratory found significant differences in scapular kinematics between the affected and unaffected sides of women reporting shoulder pain following treatment for breast cancer. An earlier smaller study from our laboratory found reduced muscle activity from four key muscles and an association with greater shoulder pain and disability. The aims of this study were to: correlate altered muscle activity from a larger sample with observed movement deviations; compare within subject movement and muscle deviations in survivors with healthy variation; explore the impact of a mastectomy vs. a wide local excision (WLE) on the observed deviations. **Method.** Cross-sectional study. One hundred and fifty-five women treated for unilateral carcinoma of the breast and 21 age-matched healthy women were included in the study. All patients filled out the Shoulder Pain and Disability Index (SPADI). Three-dimensional (3D)-kinematic data and EMG muscle activity were recorded during scaption on the affected and unaffected side. The association between kinematic data, EMG data, SPADI and covariates was determined using a two stage, random effects mixed multiple regression technique. **Results.** All scapula kinematic and muscle EMG parameters in both arms were altered in breast cancer survivors when compared to healthy participants. Altered movement patterns were different for left vs. right side affected. Mastectomy patients demonstrated greater movement deviations and reported significantly higher levels of pain than WLE patients. **Conclusion.** Shoulder morbidity is bilateral, greater in patients having a mastectomy and is present for up to six years post-surgery. This study and others now provide ample evidence to support prospective surveillance programmes that can be integrated into Survivorship Programmes.

Women treated for breast cancer often complain of shoulder pain and decreased function from surgery to six years post-surgery, 10–55% of women show restricted shoulder range of movement (ROM), 22–38% complain of shoulder pain, and 42–56% report difficulties with lifting the upper limb or reaching above the head [1–6]. These symptoms are often long lasting [7–11] and significantly reduce quality of life and the ability to return to work [7]. Recent studies comparing shoulder morbidity five to six years after surgery between women that had undergone sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) respectively reported that from 9% to 25% complained of shoulder pain, 14% to

24% experienced shoulder stiffness, 3% to 7% were unable to raise their arm above the shoulder, and 11% to 23% had shoulder or arm weakness [5,6]. In spite of this evidence rehabilitation provision is either non-existent or very limited in most European countries.

Function of the upper limb requires adequate mobility of the shoulder, including the scapula. Measurement of three-dimensional (3D) shoulder motion in asymptomatic subjects has demonstrated that the scapula upwardly rotates, posteriorly tilts and externally rotates during arm elevation [12]. However, when scapulothoracic motion is disproportionate to glenohumeral motion, the potential exists for

microtrauma and long-term pain. For example, scapula retraction has been found to cause an increase in the subacromial space, which is thought to allow improved excursion of the humeral head and the rotator cuff under the coracoacromial arch, preventing impingement [13]. It is suggested that subtle changes in this space may result in compression of the subacromial structures such as the bursa and rotator cuff during arm elevation. A recent study in our laboratory [10] found significant differences in scapular kinematics between the affected and unaffected sides of women reporting shoulder pain following treatment for breast cancer. Interestingly, these differences were found to be side dependent, that is, when the left side was affected differences were found to be greater than when the right side was affected; moreover, women with left affected shoulders demonstrated a decrease in upward rotation (UR) and external rotation (ER), and an increase in posterior tilt (PT), whereas women with right affected shoulders presented an increase in UR, PT and ER on the affected side when compared to the unaffected side. An earlier study on this population found reduced muscle activity in rhomboid, trapezius, and serratus anterior muscles on the affected shoulder compared to the unaffected side, and an association between decreased muscle activity and greater shoulder pain and disability [9]. These reports from our laboratory of movement deviations and altered muscle activity were based on a small sample and within subject comparisons and did not compare to a healthy population or carry out a group comparison for mastectomy and wide local excision (WLE).

The primary aim of this study was to evaluate whether or not the differences observed in shoulder kinematics and muscle activity between the affected and unaffected side in women following treatment for breast cancer can be explained in part by normal variation. Secondary aims were: 1) to evaluate the effect of surgery type (mastectomy vs. WLE) on the observed changes in movement and muscle activity; and 2) to look for associations between these

data and the following covariates: degree of humeral elevation and direction of movement (up/down), age, time since surgery, medical treatment protocol, shoulder pain and disability index (SPADI), chemotherapy, handedness, and whether left or right side was affected.

Method

Following Ethical clearance by the Oxfordshire Local Research Ethics Committee (A02,064), a cross sectional study comparing patients with shoulder pain treated for unilateral carcinoma of the breast and a sample of healthy women was conducted.

Participants

One hundred and fifty-five women with shoulder pain after a breast cancer operation and 21 healthy women volunteered to take part in the study. The inclusion/exclusion criteria for the group of women with a history of breast cancer surgery are listed in Table I. In the comparison group, women were included if they had no history of cancer, shoulder or neck pain on either side.

Instrumentation

Described in detail in Shamley et al. [9,10].

Kinematic data. The 3 Space Fastrak[®] 3D motion analysis system was used to measure shoulder kinematics. This system is formed by a transmitter that emits an electromagnetic field and four receivers. Within a 76 cm source-to-sensor separation the RMS system accuracy is 0.3–0.8 mm for position and 0.15 degree for orientation [14,15].

Three sensors were attached to the skin and a fourth sensor was used to digitise the subject's thorax, scapula and humerus. Global and local coordinate systems were set up as described by the International Society of Biomechanics (ISB) protocol [16].

Table I. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Unilateral carcinoma of the breast.	Reconstructive surgery
Treatment protocols:	
1) Wide local excision + radiotherapy	Current or previous history of shoulder complex trauma, surgery, pathology or dysfunction
2) Wide local excision + axillary radiotherapy + radiotherapy	Current or previous history of cervical neuropathy
3) Wide local excision + axillary clearance + radiotherapy	Lumpectomy
	Lymphoedema

Electromyography. Muscle activity of the pectoralis major, serratus anterior, rhomboids and upper trapezius muscles was measured using surface electromyography (SEMG). In standing, pre-gelled silver-silver chloride SEMG electrodes (Maersk Medical) were attached over the prepared skin sites, parallel to the muscle fibres as previously described [17]. Reference electrodes were placed on electrically neutral tissues. SEMG signal quality was verified by having the participant perform a resisted contraction in the manual muscle testing position specific to each of the muscles being tested.

Arm elevation trials

Patients were instructed to elevate their arm in the plane of the scapula (40° from the coronal plane) at a pace dictated by a metronome, where a complete cycle of elevation and depression of the arm took 8 s. A flat surface oriented in this plane guided the subject's arm through the movement. Full kinematic data of three repeated elevation and depression movements of the arm were collected. Prior to data collection the movements were demonstrated by the researcher and the patient was given three practice movements. This process was repeated with each arm, which side was measured first was randomly selected.

Shoulder pain and disability index

All patients completed the SPADI pain and disability questionnaire immediately prior to the arm elevation trials. The SPADI comprises 13 visual analogue scales, five make reference to pain and eight to disability. The SPADI questionnaire has been found to be both sensitive and reliable to measure shoulder dysfunction [18].

Reliability

Two observers blind to the SPADI questionnaire data carried out the kinematic and SEMG data collection. Reliability was assessed by carrying out a repeat of all measures on a different day for a randomly selected sample of five subjects.

Data reduction and analysis

The MotionMonitorTM software was used to simultaneously collect and synchronise shoulder SEMG and kinematic data. Furthermore, this software allowed the output from the 3 Space Fastrak[®] to be transformed into angular rotations of the scapula and the humerus relative to the trunk as determined by the ISB protocol [16]. Scapular rotation was plotted

as a dependent variable against thoracohumeral elevation as the independent variable. Analysis of the data only included thoracohumeral elevation of up to 110° , as the error of the scapular sensor increases beyond this point. In order to allow for international comparisons to be made terminology used to describe scapula motion in this report differs from our previous report and includes internal/external rotation (pro/retraction) and upward/downward rotation (lat/medial rotation). Anterior/posterior tilt remains the same.

For EMG data a normalisation reference was collected for 1 min at rest for each muscle. Following this, average root mean square (RMS) movement values minus the RMS resting value were determined. Data of all three arm elevation trials were averaged for the scapular position and muscle EMG reading at every 10° interval of thoracohumeral elevation.

Statistical analysis

Fastrak parameters for affected minus unaffected sides were the dependent variable and clinical and demographic data were the independent variables. In order to simultaneously model all three scapular motions of the same patient a two-stage, linear mixed model analogous to the model proposed by Weiner et al. (2002) was used [19]. Stage one utilised a linear mixed model fitted to each scapular motion in order to determine residuals values representing the amount of variation in that particular scapular motion that cannot be explained by collective effect of all predictor variables. In stage two each dependent variable was modelled by another linear mixed model while the residuals which were obtained in stage one were included in the model as risk factors.

General linear regression models were used to assess any differences between scapulae movements and mastectomy vs. WLE. Bland-Altman methods were used to determine intra-rater reliability for Fastrak and EMG measures.

Results

Demographic and clinical details are shown in Table II. The number of patients with left and right sides affected were closely represented. Intra-rater reliability for Fastrak and SEMG procedures was 0.98.

Kinematic data

Healthy vs. patients

Healthy scapulae showed greater ER and greater UR on the right vs. the left. These differences between

Table II. Demographic and clinical data for study sample (n = 176).

	Descriptive values
Control group	
Number	21
Age – mean years (SD)	53.10 (6.09)
Handedness	
Left	2
Right	19
Patient group	
Number	155
Duration since surgery – mean days (SD)	1143.81 (534.77)
Age – mean years (SD)	61.66 (9.13)
Affected side	
Left	
WLE	50
Mastectomy	22
Right	
WLE	56
mastectomy	22
Handedness	
Left	
WLE	11
Mastectomy	6
Right	
WLE	98
Mastectomy	39
missing	1
Dominant side affected	
Yes	79
No	75
Missing	1
Chemotherapy	
Yes	24
No	127
Missing	4
Mastectomy	21
Mastectomy + radiotherapy	12
Mastectomy + radiotherapy + axillary	14
Wide local excision + radiotherapy	60
Wide local excision + axillary radiotherapy + radiotherapy	20
Wide local excision + axillary clearance + radiotherapy	28
Total SPADI score – mean (SD)	168.10 (185.74)

left and right sides were also observed after treatment for breast cancer, however several differences were observed between patients and healthy participants. The increased IR seen on the left side in patients is accompanied by an increase in SA activity and a decrease in UT activity which contributes significantly to the difference seen between the affected and unaffected sides (Table III). The activity of these muscles was not shown to contribute to the side differences observed in healthy participants (data not shown). Having received chemotherapy further contributes significantly to the difference seen between the affected and unaffected shoulders in patients (Table III).

Patients demonstrated greater upward rotation on the affected sides compared to healthy participants ($p < 0.0001$, CI 4.82–8.51 for left hand; CI 3.91–7.70 for right hand). This increase was greater if the left side was affected and is explained in part by a decrease in PM activity and an increase in SA activity (Table IV).

Left affected shoulders showed a small increase in posterior tilt except over the critical phase of elevation/depression (80° – 120°) where affected shoulders showed a shift into anterior tilt compared to healthy shoulders but this was not statistically significant ($p > 0.1$, CI -0.82 – 2.20). Differences between the affected shoulders and healthy shoulders were mirrored on the unaffected side. That is, unaffected shoulders of patients also showed greater upward rotation (left hand $p < 0.001$, CI 4.61–8.23; right hand $p < 0.001$, CI 3.05–6.92) and decreased posterior tilt (left hand $p > 0.34$, CI -0.40 – 1.15 ; right hand $p < 0.001$, CI 0.98–2.97) than the healthy shoulders. Thus both shoulders in patients demonstrated movement deviations over and above normal variation. Differences between tilt of affected and unaffected shoulders in patients were significantly associated with pain and disability and reduced SA activity (Table V).

Mastectomy vs. WLE

Figures 1–3 represent the patterns of scapulothoracic movement during elevation and depression of the arm. Although the Mast group did not appear to contribute to the differences seen in the linear regression mixed models (Tables III–V) there are some clear differences that emerge when considering the patterns of movement and muscle activity as seen graphically at 10° intervals of arm elevation (Figures 1–3). The magnitude of IR and UR on the left affected side in the Mast group is larger than left affected WLE (IR $p < 0.001$, CI 10.4–16.56; UR $p < 0.001$, CI 2.26–7.71) (Figures 1 and 2).

Mast patients had greater upward rotation in both left and right affected shoulders compared to the unaffected, whereas in WLE patients the increase was only observed in the right affected shoulder; the left affected shoulder of WLE patients demonstrated reduced upward rotation.

The left affected shoulders of both groups of patients demonstrated increased posterior tilt (Figure 3). During the critical zone right WLE and left Mast patients show a larger shift in direction of tilt towards a more functional range.

Larger movement deviation is seen in the Mast group which also report significantly higher levels of pain ($p < 0.03$, CI 3.78–67.57).

Table III. Two stage, random effects multiple linear regression for associations between scapula internal/external rotation and covariates.

	Coef.	Std. Err.	z	p-value	95% CI	
Side affected (left)	17.69835	5.737425	3.08	0.002	6.453198	28.94349
Chemotherapy (yes)	-17.38926	7.815886	-2.22	0.026	-2.070404	-32.70812
UT effect	0.0061914	0.0017575	3.52	0.000	0.0096362	0.0027467
SA effect	0.0070949	0.0028003	2.53	0.011	0.0016064	0.0125834
Up/down rot Residuals	0.1946942	0.0139525	13.95	0.000	0.1673478	0.2220406
At/Pt Residuals	0.6427942	0.0144075	44.62	0.000	0.614556	0.6710325
Intercept	19.7621	23.09957	0.86	0.392	-25.51222	65.03642

Dependent variable: scap internal/external rotation affected - unaffected, reference category for treatment was WLE + radiotherapy. Only significant variables shown. Number of observations = 2728, Number of patients = 149, 6 observations dropped due to missing covariates. Log likelihood = -7436.63. Model p-value = 0.000.

Muscle activity

With the exception of UT in the mast group, all affected shoulders demonstrated significantly greater muscle activity on the left side when compared to the healthy left side (UT $p < 0.05$, CI 2.38–15.01 for WLE; PM $p < 0.001$, Rhom $p < 0.001$, SA $p < 0.001$, CI 6.09–12.9 for WLE and $p < 0.05$, CI 1.02–9.02 for mast). Compared to healthy shoulders, mastectomy patients demonstrated significantly increased activity in the right affected shoulders for UT ($p < 0.001$, CI 9.8–21.51), Rhom ($p < 0.001$, CI 11.1–15.71) and SA ($p < 0.001$, CI 7.16–16.26). Whereas in the case of WLE patients such increases were not observed in SA and PM activity on the right affected shoulders, where a decrease was noted. Both groups show a reversal of the healthy pattern seen in PM and SA for left and right sides.

Discussion

This paper reports altered muscle activity and shoulder kinematics in both shoulders of women treated for breast cancer compared to healthy women. Pain and movement deviations are greater in patients treated with mastectomy vs. WLE. This study has allowed us to place previous findings [9,10] in the context of normal variation and the more invasive management of mastectomy.

The results of this study would be strengthened by a larger, age matched control group.

Decreased posterior tilt and internal rotation of the scapula reported here have been noted in patients with impingement syndrome [20,21]. Evidence suggests that internal rotation of the scapula decreases the subacromial space thus resulting in a compression of the superior part of the rotator cuff and the subacromial bursa [22]. The more internally rotated position of the scapula may also cause a secondary lateral rotation of the humerus, increasing the risk of an internal impingement of the posterior part of the rotator cuff [23]. It is also postulated that increased anterior tilt further compromises the subacromial space, resulting in external impingement [24]. In our study decreased posterior tilt was associated with high levels of reported pain.

The increased upward rotation of the scapula in our patient groups is in agreement with the findings of Crosbie et al. [25] who reported an increase in upward rotation of the scapula following mastectomy for breast cancer. This is believed to represent a compensatory mechanism for a dysfunctional motion of the glenohumeral joint [23]. This altered scapulo-humeral rhythm has been observed in patients with shoulder capsulitis [26] and full-thickness rotator cuff tears [27]. Where stiffness of the glenohumeral joint or an inability of the rotator cuff to efficiently move the head of the humerus is present, patients appear

Table IV. Two stage, random effects multiple regression for associations between scapula upward/downward rotation and covariates.

	Coef.	Std. Err.	z	p-value	95% CI	
Upward arm movement	-0.5263677	0.1575948	-3.34	0.001	-0.8352477	-0.2174876
Humeral elevation	0.0196792	0.0028419	6.92	0.000	0.0141092	0.0252492
Side affected (left)	-3.822779	1.612783	-2.37	0.018	-6.983776	-0.6617822
PM effect	-0.0122696	0.0041855	-2.93	0.003	-0.020473	-0.0040661
SA effect	0.0110035	0.0039594	2.78	0.005	0.0032432	0.0187637
Int/Ext rot Residuals	0.3615268	0.0258706	13.97	0.000	0.3108214	0.4122322
At/Pt Residuals	-0.2983994	0.0254423	-11.73	0.000	-0.3482654	-0.2485334
Intercept	-5.851908	6.497204	-0.90	0.368	-18.58619	6.882377

Dependent variable: scap upward/downward rotation affected - unaffected, reference category for treatment was WLE + radiotherapy. Only significant variables shown. Number of observations = 2728, Number of patients = 149, 6 observations dropped due to missing covariates. Log likelihood = -8041.82. Model p-value = 0.000.

Table V. Two stage, random effects multiple regression for associations between scapula anterior/posterior tilt and covariates.

	Coef.	Std. Err.	z	p-value	95% CI	
Upward arm movement	0.2815034	0.1188529	2.37	0.018	0.048556	0.5144508
Spadi Pain effect	0.0477709	0.0231911	2.06	0.039	0.0023171	0.0932247
Spadi disab. Effect	-0.0490682	0.0221916	-2.21	0.027	-0.092563	-0.0055733
Wleaxcl Treatment	9.178385	4.501797	2.04	0.041	0.3550238	18.00175
SA effect	0.0096405	0.0029959	3.22	0.001	0.0037688	0.0155123
Int/Ext rot Residuals	0.6787733	0.0151915	44.68	0.000	0.6489985	0.708548
Up/down rot Residuals	-0.1697199	0.0144681	-11.73	0.000	-0.1980768	-0.141363
Intercept	-7.209109	9.02434	-0.80	-0.424	-24.89649	10.47827

Dependent variable: scap anterior/posterior tilt affected - unaffected, reference category for treatment was WLE + radiotherapy. Only significant variables shown. Number of observations = 2728, Number of patients = 149, 6 observations dropped due to missing covariates. Log likelihood = -7362.99. Model p-value = 0.000.

to compensate by increasing the amount of scapula upward rotation during elevation of the arm.

Changes in scapula kinematics compared to healthy subjects were seen to a greater extent in patients following a mastectomy, and were even greater if the affected shoulder of mastectomy patients was the left. Whilst the statistical analysis of Crosbie et al. [25] did not specifically differentiate between left affected and right affected shoulders, the authors acknowledge from the interpretation of their results that kinematic changes were greater on left affected sides. Mastectomy patients also demonstrated significantly greater pain than patients treated with a WLE.

Since left affected mastectomy shoulders demonstrated greatest pain, the different patterns of

movement on the left may represent the greater need for compensatory scapular motion. In both patient groups internal rotation was increased on the left side whereas it was decreased on the right. Thus the increased internal rotation on the left might contribute to the greater presence of pain on the left side by causing either an internal or external impingement as stated above. In our previous paper [10], when all patients were analysed together, we found decreased upward rotation in the left affected side, our subgroup analysis reported in this paper allows us to conclude that the difference was caused by the decrease in upward rotation observed in the left side of WLE patients. Interestingly, the changes in posterior tilt and upward rotation described for the affected shoulder were also seen in the unaffected shoulders

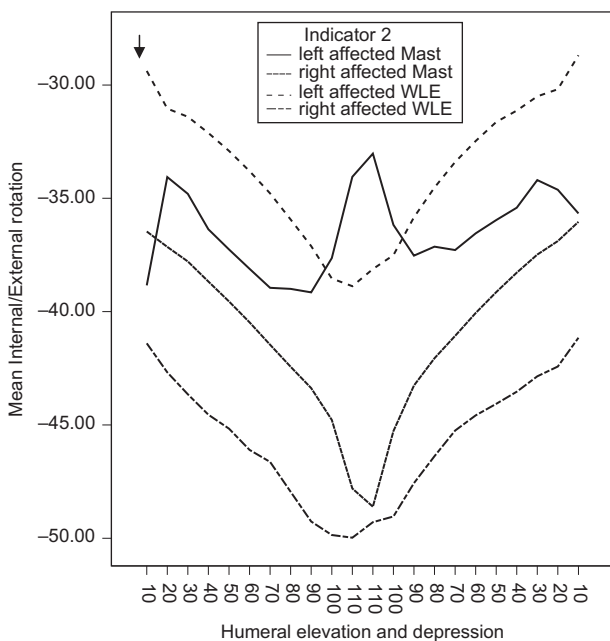


Figure 1. Mean scapula internal/external rotation plotted against humeral elevation and depression for mastectomy and wide local excision (WLE) patients. Arrow represents direction of external rotation.

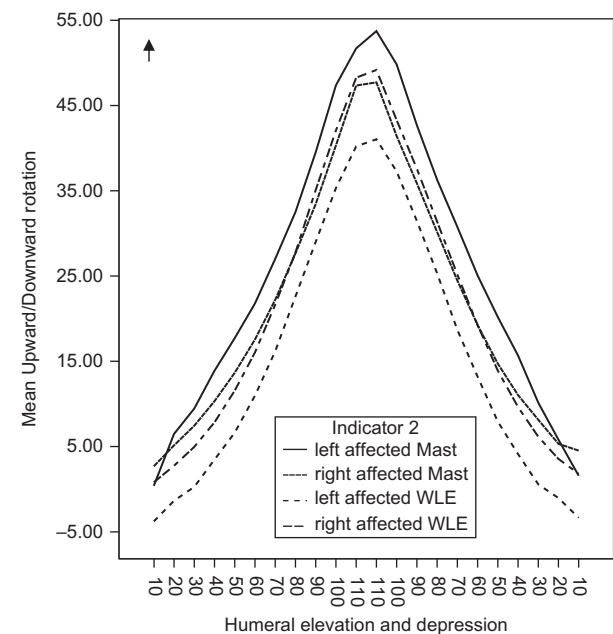


Figure 2. Mean scapula upward/downward rotation plotted against humeral elevation and depression for mastectomy and wide local excision (WLE) patients. Arrow represents direction of upward rotation.

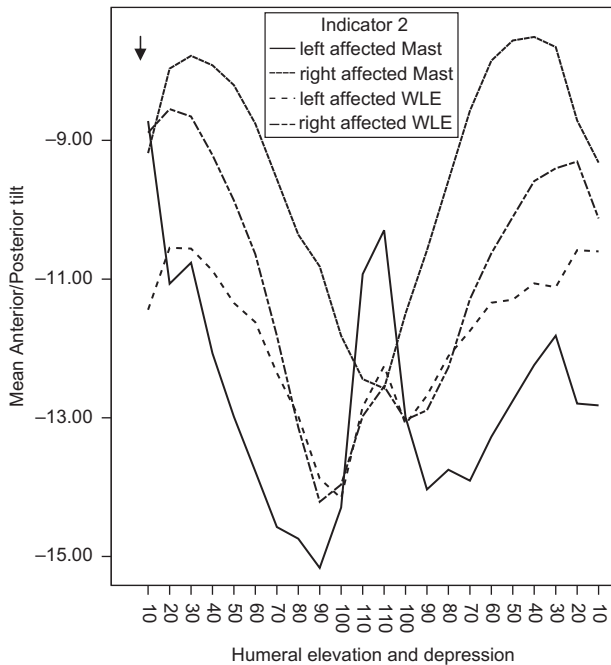


Figure 3. Mean scapula posterior/anterior tilt plotted against humeral elevation and depression for mastectomy and wide local excision (WLE) patients. Arrow represents direction of posterior tilt.

of patients. Similar findings were also reported by Crosbie et al. [25] who found a bilateral increase in upward rotation in patients following unilateral mastectomy.

UT and SA function as a force couple to rotate the scapula in an upward direction [28], therefore an increase in the activity of these muscles in a patient population that show increased upward rotation of the scapula appears reasonable. The finding of increased UT activity in patients with shoulder dysfunction is quite consistent among the literature and has been observed in patients with impingement [20] and frozen shoulder [29]. In contrast, and unlike our study that found increased SA activity, studies assessing shoulder pathologies have reported a decrease in SA activity [20]. This may be explained by the fact that these studies reporting decreased SA activity also reported a decrease in upward rotation of the scapula.

PM activity may be contributing to the increased level of pain seen in the Mast group. Increased PM activity in this group was accompanied by greater changes in scapular internal rotation and posterior tilt compared to healthy subjects, especially on the left side. It is well known that PM has an anterior tilting and internal rotating effect on the scapula [30].

Large differences between the affected shoulder of both patient groups and healthy subjects were observed with regards to RH activity. RH is an external

rotator of the scapula [30], and despite the fact that RH activity was substantially increased in the affected shoulders, these still remained internally rotated when compared to healthy shoulders; this may be a reflection of decreased myofascial tissue extensibility of the anterior part of the pectoral girdle and the axilla in patients following treatment for breast cancer.

In line with the findings regarding scapular kinematics, EMG differences between patients and healthy subjects were mirrored on the asymptomatic shoulder of patients. There is evidence in the literature for the occurrence of this phenomenon [31], which suggests an effect in the central nervous system that results in the reorganisation of motor control and movement patterns. However, these patients have received treatment with known systemic effects and as such the potential for cancer treatment to induce bilateral morbidity via changes in circulating levels of cytokines and growth factors (GF) cannot be ignored.

Indeed, the role of inflammatory cytokines and GF in the development of shoulder conditions such as rotator cuff disease, impingement and adhesive capsulitis (frozen shoulder) is a growing area of research which has not examined these factors in relation to co-morbidities such as breast cancer [32,33]. Given we have identified movement patterns in breast cancer patients that mimic these shoulder conditions it seems feasible to place this evidence in the context of current biomedical research.

A relationship between IL-1, IL-1 β , COX-1, COX-2, substance-P, subacromial bursitis and rotator cuff disease has been shown by several authors [34,35]. Sakai et al. [36] have shown marked hyperplasia of the blood vessels and fibroblasts of subacromial bursa in patients with rotator cuff tendonitis compared to patients with anterior instability. IL-1, TNF- α , bFGF and TGF- β were all over expressed in blood vessels and fibroblast cytoplasm. TGF- β was the only one that showed increased staining in the matrix and is a potent immunosuppressive cytokine whose levels undergo significant elevation after radiation therapy both in the short term (three weeks) and in the longer term (up to one year) [37]. Irradiation is known to result in overproduction of proinflammatory mediators which leads to both vascular injury [38] and activation of the inflammatory cascade [39]. The associated cytokines released then participate in a number of physiological responses, which include the pain response and the development of fibrosis.

Less is known about the effects of chemotherapy on healthy tissues but there are general side effects associated with most forms of chemotherapy including fatigue, bilateral joint pain and myalgia. Our

results show a significant association between chemotherapy and a number of altered patterns of movement.

In order to target at risk groups future research must attempt to elucidate the relevance of candidate markers of radiotherapy and chemotherapy damage in the development of shoulder pain and dysfunction.

Conclusion

Shoulder morbidity is bilateral, greater in patients having a mastectomy and is present for up to six years post-surgery. This study and others now provide ample evidence to support prospective surveillance programmes that can be integrated into Survivorship Programmes. In the absence of dedicated resources creative use of triage systems, DVDs and online self-assessment and self-referral pathways must be considered if we are to meet the needs of this patient group.

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