A preliminary study of manipulation under anaesthesia for secondary frozen shoulder following breast cancer treatment

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ABSTRACT
INTRODUCTION The aim of this paper is to present the results of manipulation under anaesthesia (MUA) and injection of local anaesthetic and corticosteroid followed by a physiotherapy regime for secondary frozen shoulder after breast cancer treatment (surgery, radiotherapy), and to compare them with a control group.

METHODS Patients referred to the senior author for secondary frozen shoulder following breast cancer treatment over a ten-year period were investigated. Recorded data included age, treatment for breast cancer, length of symptoms, Oxford shoulder score (OSS) and range of motion before and after shoulder MUA. These data were compared with a control group of patients with frozen shoulder.

RESULTS A total of 263 patients were referred with 281 frozen shoulders. Of these, 7 patients (7 shoulders) had undergone previous breast cancer treatment and the remaining 256 patients (274 shoulders) formed the control group. None of the patients were diabetic. The mean preoperative OSS was 31 for the study group and 27 for the control group, improving to 43 for both groups following MUA. Forty-two per cent of the study group and fifteen per cent of the control group had a second MUA subsequently. At the long-term follow-up appointment, 71% of the study group patients were satisfied with their result.

CONCLUSIONS The results of this preliminary study suggest that MUA, corticosteroid injection and subsequent physiotherapy have achieved good final results in a series of patients with frozen shoulder secondary to breast cancer treatment. Members of the multidisciplinary team looking after breast cancer patients should be aware of this management option and, on manifestation of this pathology, should refer the patient to an orthopaedic surgeon.

KEYWORDS
Frozen shoulder – Manipulation under anaesthesia – Breast cancer – Mastectomy – Radiotherapy

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Breast cancer is the most common malignant disease in women, accounting for 1.4 million new cases per year. In the UK, it is estimated that the lifetime risk for women of developing breast cancer is 1 in 8. Advancements in the treatment of breast cancer have resulted in documented survival rates with over 75% of women diagnosed with breast cancer expected to live for at least ten years. This increased rate of breast cancer survivors renders it imperative for the physicians to manage the consequences of the often aggressive cancer treatments (surgical, radiotherapy, chemotherapy).

Shoulder morbidity is a recognised complication following breast surgery and/or subsequent radiotherapy. The most documented cause of morbidity is shoulder stiffness, pain and the development of adhesive capsulitis, also known as frozen shoulder. The prevalence can be as high as 86% of patients treated for breast cancer, with Ewertz and Jensen reporting that 55% of Danish patients had reduced arm and shoulder function three years following cancer treatment. Greater impairment has been documented for mastectomy as opposed to wide local excision and for radiotherapy as opposed to non-radiotherapy.

Frozen shoulder is a well recognised pathology characterised by painful selective restriction of passive and active movements of the shoulder in the presence of normal radiography. The majority of cases are idiopathic. Nevertheless, there is a described group of those with secondary frozen shoulder where a clear primary precipitating cause such as surgery or trauma to the shoulder can be identified. Frozen shoulder can be managed with a variety of interventions including physiotherapy and steroid injections to manipulation under anaesthesia (MUA) and arthroscopic capsular release.

The aim of this paper is to present the results of MUA and injection of local anaesthetic and corticosteroid for secondary frozen shoulder following breast cancer treatment, and to compare them with the results of MUA in a control group with frozen shoulder. Several studies have focused on the effect of different physiotherapy regimes in breast
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cancer survivors in order to minimise the prevalence of shoulder morbidity and frozen shoulder in particular. To our knowledge, this is the first study addressing the effect of shoulder MUA for secondary frozen shoulder in breast cancer survivors.

Methods

A consecutive series of patients who were referred to the senior author for secondary frozen shoulder following breast cancer treatment was identified retrospectively and reviewed. Once the referral was made and the diagnosis of secondary frozen shoulder was established, the patient was listed for shoulder MUA and injection at the next available elective list.

Collected data included age, treatment for breast cancer and length of symptoms as well as shoulder range of motion (ROM) (abduction, forward flexion, internal rotation, external rotation) before shoulder MUA. All the patients completed an Oxford shoulder score (OSS) assessment on the first outpatient department appointment and on the day of admission before the MUA.

General anaesthetic was administered with the patient supine and an initial assessment of the passive ROM was conducted with the patient's scapula fixed. Subsequently, manipulation was performed in the following order: abduction, flexion, external rotation, cross-body adduction and internal rotation. The manoeuvres were repeated until the maximum ROM was achieved. All the measurements were conducted by eye by the senior author. Finally, the gleno-humeral joint was injected with 10ml of 0.5% bupivacaine and 80mg of methylprednisolone using a direct anterior approach.

All patients were offered a standardised physiotherapy regime followed by passive and active rehabilitation. The programme commenced in the hydrotherapy pool within 48 hours of the procedure and progressed to land-based exercises. This regime was continued until both the patient and the physiotherapist were happy that further improvement was not possible. Each patient received one hydrotherapy and three land-based physiotherapy sessions before discharge.

All patients were reviewed in the outpatient department within six weeks of surgery, and until both the patient and the senior author were happy with the clinical outcome. Further MUA was offered if there was patient dissatisfaction in combination with recurrence or persistence of limited ROM. Long-term follow-up consisted of an outpatient attendance and a final recorded OSS.

Table 1 Details of patients included in the cancer treatment group

| Age | Type of treatment | Length of symptoms before MUA (weeks) | OSS prior to MUA | OSS following MUA | 2nd MUA? | Time to 2nd MUA (weeks) | OSS prior to 2nd MUA | OSS following 2nd MUA | Final outcome / OSS |
|-----|-------------------|--------------------------------------|-----------------|-----------------|---------|----------------------|-------------------|---------------------|---------------------|
| 54  | WLE + AC + radiotherapy (50Gy, 25 fractions, 5 weeks) | 40                     | 33              | 47              | No      |                      |                    |                     | Improvement / 44    |
| 50  | Mastectomy + AC + radiotherapy (50Gy, 25 fractions, 5 weeks) | 100                    | 34              | 35              | No      |                      |                    |                     | Pending arthroscopy / 27 |
| 60  | Mastectomy + radiotherapy (50Gy, 25 fractions, 5 weeks) | 52                     | 27              | 34              | Yes     | 4                    | 36                | 46                  | Shoulder replacement / 17 |
| 41  | Mastectomy + radiotherapy (50Gy, 25 fractions, 5 weeks) | 43                     | 20              | 48              | No      |                      |                    |                     | Improved / 36       |
| 43  | Mastectomy + radiotherapy (50Gy, 25 fractions, 5 weeks) | 50                     | 29              | 42              | Yes     | 40                   | 40                | 37                  | Improved / 37       |
| 49  | Mastectomy + radiotherapy (50Gy, 25 fractions, 5 weeks) | 52                     | 32              | 45              | Yes     | 156                  | 32                | 45                  | Improved / 45       |
| 43  | WLE + AC          | 40                     | 44              | 47              | No      |                      |                    |                     | Improved / 45       |

MUA = manipulation under anaesthesia; OSS = Oxford shoulder score; WLE = wide local excision; AC = axillary clearance
Results
Between January 1999 and January 2009, 281 consecutive frozen shoulders (263 patients) were referred to the senior author. Our study group included seven patients (seven shoulders) who had had previous breast cancer treatment. The remaining 256 patients (274 shoulders) formed the control group. None of the study or control group patients were diabetic.

The study group comprised seven women with seven frozen shoulders secondary to breast cancer treatment. At the time of the MUA, the mean age of the patients was 48 years (range: 41–60 years). The mean time of shoulder symptoms before MUA was 54 weeks (range: 40–100 weeks). Six of the seven patients had surgical treatment as well as radiotherapy for breast cancer while one had only surgical treatment. The age, treatment regime for breast cancer, OSS, time to MUA and the final outcome of the study group are demonstrated in Table 1.

The control group consisted of 256 patients (274 shoulders). Among these patients, 114 were male and 142 female, and the mean age was 51 years at the time of MUA (range: 27–81 years). Primary frozen shoulder was present in 214 cases and secondary frozen shoulder in 60 cases. A total of 271 shoulders (99%) were assessed at the initial follow-up appointment and 229 shoulders (84%) were available for long-term follow-up (mean: 3.6 years, range: 0.7–10.6 years).

Following the first MUA, the change in OSS, the ROM prior to the MUA and the ROM following the MUA are demonstrated in Table 2. The results between the control group and the study group were comparable. Three of the seven patients (42%) in the study group had a subsequent second MUA. None of the patients underwent further MUAs. In the control group, 42 patients (15%) underwent a second MUA.

At the long-term follow-up visit, five of the seven patients (71%) were satisfied with their final result, which was reflected in their increased OSS and ROM. Two patients (29%) needed further procedures; one a shoulder arthroscopy and one a shoulder replacement as she developed osteoarthritis of the glenohumeral joint. The mean OSS in the study group was 53 (range: 17–45). In the control group, the mean OSS at the long-term follow-up appointment was 45 (range: 11–48).

Discussion
The results of this preliminary study suggest that MUA and corticosteroid injection followed by physiotherapy can achieve satisfactory outcomes in the management of frozen shoulder secondary to surgical treatment and/or radiotherapy for breast cancer. Radiotherapy inevitably affects surrounding healthy tissues apart from the targeted tumour cells. Late tissue complications of radiotherapy include fibrosis, which is the excessive accumulation of collagen and other extracellular matrix (ECM) following an imbalance of ECM synthesis and degradation. Fibrosis occurs through a pathway that involves activation of proinflammatory and profibrotic cytokines, leading eventually to an inflammatory response and increased collagen deposition.11–13

More specifically, in response to endothelial or epithelial cell injury caused by radiotherapy, transforming growth factor beta (TGF-β) is released. TGF-β promotes the migration of fibroblasts as well as their differentiation into myofibroblasts.14–16 Myofibroblasts are producers of collagen and other ECM. They are also activated by cytokines, which are released from the accumulated inflammatory cells (neutrophils, macrophages, monocytes and lymphocytes) as a result of radiotherapy induced cellular damage. Together with the vasodilation and angiogenesis following radio-
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therapy trauma, this activation of myofibroblasts can lead to increased ECM deposition and subsequent fibrosis.11–13 Tissue fibrosis causes pain, restriction of ROM and secondary frozen shoulder.

Hopwood et al reported a 20% prevalence of moderate or marked shoulder stiffness at five years following surgery for patients who had undergone radiotherapy for breast cancer.14 As opposed to chemotherapy, radiotherapy regimes are mainly designed empirically with very few published studies assessing the maximum tissue tolerance of radiotherapy in balance with tumour eradication.15

The importance of prevention of adverse shoulder morbidity following radiotherapy has been addressed by Hopwood et al in two randomised controlled trials (RCTs) assessing different radiotherapy regimes and doses.14 In the first trial, the authors compared the adverse effects of two hypofractionated radiotherapy regimes (41.6 Gy and 50 Gy in 15 fractions over 5 weeks) against the international standard dose of 50 Gy delivered in 25 fractions over 5 weeks. In the second trial, the effects of the standard dose were compared with a regime delivering 40 Gy in 15 fractions over 5 weeks. The results of these trials demonstrated that shoulder symptoms (pain, stiffness and decreased ROM) did not differ in a statistically significant way between the examined regimes at a maximum follow-up of five years.

These findings are supported by another RCT published in 2012 by Versmessen et al comparing the standard dose with a regime delivering 42 Gy in 15 fractions over 5 weeks.15 The authors concluded that the two radiotherapy regimes did not have any statistically significant difference in the development of shoulder and arm symptoms at a maximum follow-up of three years. The aforementioned trials14,15 concluded that shoulder pain and stiffness is not affected by either a higher dose regime or a lower dose at each fraction, which could be an indication that even low doses of radiation are sufficient to create significant soft tissue damage.

Common surgical treatments for breast cancer include mastectomy, wide local excision, sentinel lymph node biopsy and axillary clearance. They have all been associated with the development of secondary frozen shoulder as reported both by patients and clinicians. More specifically, in one study, 75% of women reported decreased shoulder ROM, pain and resultant limitation of their daily activities following surgical management of breast cancer.5 Furthermore, Leidenius et al reported objectively decreased shoulder ROM in 45% of patients following sentinel node biopsy and in 86% of the patients who subsequently underwent axillary clearance.7 The trigger pathogenetic factor for the development of secondary frozen shoulder in this group of patients could be a combination of incisional/surgical pain leading to voluntarily or subconsciously limited ROM as well as the initiation of an inflammatory cascade following surgical trauma, resulting in fibroblast activation and ECM deposition via the same pathway as with the aforementioned radiotherapy fibrosis.5,8,13–15

Greater surgical trauma could result in a more significant fibrotic response. This hypothesis could potentially explain the higher prevalence of secondary frozen shoulder in patients following mastectomy as opposed to wide local excision and in axillary clearance as opposed to sentinel node biopsy only.3,15 Moreover, in patients who have undergone radiotherapy, there is a higher prevalence of secondary frozen shoulder than in patients who did not.3

Among physicians, there is no clear consensus in the management of shoulder stiffness and pain following breast cancer treatment. Several studies have addressed the efficacy of different physiotherapy regimes in the management of this pathology. Kilbreath et al conducted a RCT that demonstrated that a progressive physiotherapy regime following breast cancer surgery resulted in increased shoulder ROM in the study group.16 This was confirmed in a further RCT by Beurskens et al, highlighting the beneficial role of physiotherapy on shoulder ROM following surgical management of breast cancer.8 It is of note that there are no studies describing the effect of surgical management (including MUA or arthroscopic capsular release) for secondary frozen shoulder in breast cancer survivors.

The prevalence of shoulder stiffness and pain in patients following surgical treatment and/or radiotherapy for breast cancer has been well documented in the literature.13–14 Nevertheless, within the ten years of data collection, only seven patients with frozen shoulder secondary to breast cancer treatment were referred to the senior author. This is potentially a reflection of the absence of consensus for the management of this pathology as well as the fact that health professionals dealing with breast cancer survivors are not aware of this treatment option for secondary frozen shoulder.

The main advantage of our study is that to our knowledge, it is the first study assessing the results of shoulder MUA in breast cancer survivors and comparing them with a large control group. Furthermore, none of the patients in either the study or the control group were diabetic and so diabetes as a bias factor for the development of frozen shoulder was excluded. The main disadvantage is the small number of patients in the study group.

Conclusions

Our results suggest that MUA and corticosteroid injection followed by a structured physiotherapy regime can achieve good final results in patients with frozen shoulder secondary to treatment for breast cancer. In order to reach a good outcome, certain patients required repeat MUA. The results of the study group were comparable with those of the control group. We therefore advocate treating frozen shoulder following breast cancer treatment in the same way as for the control group. This was a preliminary study that aimed to introduce this management option for secondary frozen shoulder to the members of the multidisciplinary team looking after breast cancer patients. Larger patient data are required in order to confirm the aforementioned findings.

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