Health Policy Advisory Committee on Technology

Technology Brief

InSpace™ biodegradable subacromial spacer for rotator cuff tears

March 2015
Technology, Company and Licensing

Register ID  WP211
Technology name  InSpace™ biodegradable subacromial spacer
Patient indications:  Patients with scarred or torn tendons due to trauma or degradation, absence of tendon or muscle or non-functional tendon or muscle and ruptured tendons.

Description of the technology

The InSpace™ (Ortho-Space Ltd, Caesarea, Israel) biodegradable subacromial spacer (Figure 1) is intended to decrease the pain associated with a rotator cuff tear by creating a physical barrier (spacer) between tissues in the subacromial space, thus reducing friction between the acromion (the bone on top of the shoulder) and the humeral head (top of the upper arm bone). As pain associated with ruptured tendons may cause abnormal motion and hinder rehabilitation, reducing this pain may facilitate recovery, improve shoulder function and potentially eliminate or defer the need for more extensive shoulder surgery. The device, which is made from a biodegradable polymer, gradually dissolves following implantation and is completely absorbed within one year. The spacer is available in three sizes; small (40 x 50 mm), medium (50 x 60 mm) and large (60 x 70 mm).¹

Implantation of the InSpace biodegradable spacer is conducted under general or regional anaesthesia using minimally invasive techniques such as arthroscopy or mini-open surgery. During the procedure the balloon, that is supplied folded into a cylinder-shaped insertion tube (deployer), is implanted between the acromion and humeral head, inflated using saline and then sealed. It usually takes less than 10 minutes from introduction of the device to sealing and retraction of the deployer. Usually, the patient is able to go home the same day of surgery. Use of a sling is recommended for one week after surgery.¹

Contraindications to using the InSpace biodegradable subacromial spacer include:

- an active or latent infection or signs of tissue necrosis in the shoulder;
- an allergy to the balloon material;
- a blood coagulation disorder, a compromised immune system, severe/unstable chronic disease such as heart failure, cirrhosis, chronic renal failure or any other condition that may compromise wound healing.¹
Company or developer
Ortho-Space Ltd, Caesarea, Israel.

Reason for assessment
The InSpace biodegradable subacromial spacer offers a less invasive and safer alternative to major surgery with shorter procedure and rehabilitation times, and provides an option for patients with large rotator cuff tears that cannot be repaired by conventional means.

Stage of development in Australia
- ☒ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☐ Nearly established
- ☐ Established
- ☐ Established but changed indication or modification of technique
- ☐ Should be taken out of use

Licensing, reimbursement and other approval
The InSpace biodegradable subacromial spacer received the CE mark in July 2010\textsuperscript{1}, but it has not been approved by the United States Food and Drug Administration or the Australian Therapeutic Goods Administration.

Australian Therapeutic Goods Administration approval
- ☒ Yes
- ☐ No
- ☐ Not applicable

\textsuperscript{1} ARTG number (s)
Patient Indication and Setting

Disease description and associated mortality and morbidity

The rotator cuff is a group of four muscles in the shoulder connected via tendons to the upper arm bone (humerus). These muscles are responsible for the arm’s movement, primarily the ability to lift and rotate. A lubricating sac, or bursa, separates the rotator cuff from the bone at the top of the shoulder (acromion) and allows the muscles to glide smoothly. A rotator cuff tear refers to a split in one or more of the muscles or tendons that make up the rotator cuff. Tears are classified as either partial or full thickness. Partial-thickness tears involve only a portion of the tendon thickness. Full-thickness tears refer to a complete severance of rotator cuff fibres, which allows contact between the arm bone and the bursa, causing the latter to become inflamed and painful. Tears are further rated as small (<1 cm), medium (1–3 cm), large (3–5 cm) and massive (>5 cm). Tears that involve two or more tendons may also be classified as massive. Irreparable rotator cuff tears are those that, because of their size, are not reparable by conventional means. Assessment of rotator cuff tears is done using X-ray, ultrasound and magnetic resonance imaging.

Rotator cuff tears may result from a single traumatic injury (e.g. a fall), degeneration over a period of years due to over-use of the muscles and tendons, or the normal wear and tear associated with aging. They also occur in the shoulders of athletes, particularly in those whose sport involves a repetitive overhead or throwing action (e.g. tennis).

Rotator cuff tears are not a life-threatening condition, but cause pain, loss of arm function and weakness. The pain is often worse at night, especially when lying on the shoulder, and may result in sleep disturbance. People with rotator cuff tears have difficulty performing overhead tasks, getting dressed, reaching back pockets, and generally maintaining physical employment or participating in recreational activities. A shoulder disorder can increase functional dependency in the elderly due to difficulties in completing activities of daily living. In younger adults this morbidity may lead to absenteeism from work and lost productivity. Once a tear occurs, it is unlikely to heal and tends to increase in size over time. Left untreated, large tears may result in a chronic hole in the muscle-tendon unit and shrinkage (atrophy) of the muscles, which may undergo fatty degeneration, a potentially irreversible process that results in permanent arm weakness.

The incidence of rotator cuff tears increases with age. Full-thickness rotator cuff tears are rare before the age of 60 years (less than 6 per cent), but are present in up to 50 per cent of 70-year olds.
Number of patients
In a population-based study in Australia, 22.3 per cent of participants reported shoulder pain or stiffness.⁷ Studies from the Australian “Bettering the Evaluation and Care of Health” (BEACH) dataset revealed that in 2012–13 the number of people presenting to a general practitioner (GP) with shoulder syndrome (includes rotator cuff syndrome) or a shoulder complaint was 1.3 per 100 GP encounters, and that the number of patients presenting with shoulder symptoms or complaints had increased by about 30 per cent between 2003–04 and 2012–13.⁸

According to the Australian Institute of Health and Welfare procedural data cubes, the number of rotator cuff repairs performed in 2011–12 was 2,355 and the number of rotator cuff repairs with decompression of the subacromial space was 3,466.⁹ No New Zealand data was identified on the number of people undergoing rotator cuff repairs. In addition, no Australian or New Zealand data was identified on the number of hemiarthroplasty or arthroplasty procedures performed specifically for irreparable rotator cuff tears.

Speciality Orthopaedics
Technology setting General hospital

Impact

Alternative and/or complementary technology
The InSpace biodegradable subacromial spacer is a substitution technology. It is an alternative to major surgery, predominantly in patients with difficult-to-treat (irreparable) rotator cuff tears, and an alternative to reverse total shoulder arthroplasty.¹

Current technology
For most patients with rotator cuff tears, with few exceptions, non-surgical treatment is recommended initially, including pain management (simple analgesics, anti-inflammatory medications and subacromial corticosteroid injections), activity modification, and strength-based physiotherapy programs for six weeks to three months. The success rate for non-surgical treatments varies from less than 50 per cent to more than 90 per cent.², ⁴

For patients who do not improve with non-surgical treatment or who have acute, large, traumatic tears, such as those caused by shoulder dislocation with associated tendon detachment, surgery may be offered to repair the tendons. Surgery may be open, mini-open or arthroscopic. Regardless of the approach, surgical repair involves suturing the torn edges of the involved tendon(s) together and reattaching the tendon to the humeral head. A full or partial repair may be performed, depending on the severity of the tear.², ⁴

Other procedures often performed in combination with rotator cuff repair include debridement (removal of soft tissue and bone fragments that may be connected to the
bone) and acromioplasty (removal of bone from the underside of the tip of the shoulder blade to give the tendon more movement space). In addition, subacromial decompression may be performed, which combines an acromioplasty with removal of the subacromial bursa and, in some cases, removal of the coracoacromial ligament. The re-tear rate of massive tears after primary repair ranges from 20 per cent to 65 per cent.

For patients with irreparable rotator cuff tears (i.e. have marked tendon atrophy plus advanced fatty degeneration of the muscles) and significant pain and disability, different salvage operations can be performed. These include:

- tendon transfers (where large chest wall muscles are transferred to replace lost rotator cuff function);
- hemiarthroplasty (a replacement or resurfacing of the humeral head);
- reverse total shoulder arthroplasty (reverses the normal shoulder anatomy to provide stability and deltoid tension in the absence of a rotator cuff).

There is no consensus or definitive guidelines concerning the preferred surgical option designed to treat massive, irreparable rotator cuff tears when non-surgical treatments have failed.

A complication rate of 19.5% and a re-operation rate of 11.9% has been reported for patients undergoing reverse total shoulder arthroplasty for rotator cuff tears. The main types of complications are post-operative instability, infection and glenoid loosening. Complications rates for reverse total shoulder arthroplasty are similar to those for hemiarthroplasty with respect to 30 day lower respiratory tract infection, myocardial infarction, pulmonary embolism ad 90 day in-patient mortality. Surgery for reverse total shoulder arthroplasty or hemiarthroplasty usually takes about two hours, with patients in hospital for two to three days. Recovery for reverse total shoulder arthroplasty can take three to six months, with patients required to wear a sling for up to six weeks following the operation.

A systematic review on latissimus dorsi tendon transfer for irreparable rotator cuff tears reported an overall complication rate of 9.5% and a re-operation rate of 6.9%. Complications included tears of the transferred tendon (3.4%), neuropraxia (2.7%), wound dehiscence (1.5%), failure of deltoid repair (0.7%), haematomas (0.7%) and infection (0.4%). Recovery involves four to six weeks of immobilisation in a rigid orthosis with the arm in slight abduction.

**Diffusion of technology in Australia**

There is limited use of the InSpace biodegradable subacromial spacer in Australia (personal communication, Ortho-Space Ltd).
International utilisation

The InSpace biodegradable subacromial spacer is being used in various European countries with nearly 4,000 implantations accomplished to date (personal communication, Ortho-Space Ltd).

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of Use</th>
<th>Trials underway or completed</th>
<th>Limited use</th>
<th>Widely diffused</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Switzerland</td>
<td>✓</td>
<td></td>
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<tr>
<td>France</td>
<td>✓</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Slovenia</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Greece</td>
<td>✓</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Turkey</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>✓</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Cost infrastructure and economic consequences

The device is reported to cost USD 2,000 (personal communication, Ortho-Space Ltd). Current surgical options for irreparable rotator cuff tears include hemiarthroplasty and total reverse shoulder arthroplasty. These procedures are invasive, requiring around two hours to complete and one to three nights stay in hospital. In comparison, implantation of the InSpace biodegradable subacromial spacer can be performed in an outpatient setting under general or regional anaesthesia using an arthroscopic approach. Device positioning takes less than 10 minutes from introduction of the device to sealing and retraction of the deployer. Owing to the shorter procedure and recovery periods, use of the InSpace biodegradable subacromial spacer may potentially reduce hospital costs and free-up hospital resources compared to arthroplasty procedures.

With respect to reparative surgery for rotator cuff tears, InSpace would require the same hospital stay as standard techniques and thus would be a more expensive procedure based on the USD 2,000 cost of the device (personal communication, Clinical expert).
Ethical, cultural, access or religious considerations

No cultural, religious, or access considerations for the InSpace biodegradable subacromial spacer were identified.

Evidence and Policy

Safety and effectiveness

Two studies were eligible for inclusion in this Technology Brief. Both were prospective case series (level IV interventional evidence); one was in the form of a conference abstract. Study details for the two included studies are presented in Table 1.

Table 1  Characteristics of included studies

<table>
<thead>
<tr>
<th>Study/ Design</th>
<th>Inclusion criteria</th>
<th>Number of patients</th>
<th>Duration of follow-up</th>
<th>Losses to follow-up</th>
<th>Conflicts of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senekovic et al 2013</td>
<td>Massive irreparable rotator cuff tears</td>
<td>20</td>
<td>3 years</td>
<td>3 patients</td>
<td>One or more of the authors of the study received grants or outside funding from OrthoSpace Ltd. In addition, OrthoSpace Ltd paid or directed, or agreed to pay or direct, benefits to a research fund, foundation, educational institution or other charitable or non-profit organisation with which the authors were affiliated or associated. Two of the study authors had a financial interest in OrthoSpace Ltd.</td>
</tr>
<tr>
<td>Slovenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of Evidence: IV</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naggar 2013*</td>
<td>Massive irreparable rotator cuff tears</td>
<td>21 (equal to 22 shoulders in total as one patient had both shoulders operated on)</td>
<td>mean 24 months</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Level of Evidence: IV</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

* Conference abstract; NR, not reported

Senekovic et al 2013

A prospective case series reported on the safety profile and functional results for 20 patients (11 men and 9 women; mean age 70.5 years [54 to 85]) who received an InSpace biodegradable subacromial spacer for massive irreparable rotator cuff tears.

It is not stated whether the patients were enrolled consecutively. All patients had persistent pain for at least six months, with documented failure of conservative treatment. The device was inserted arthroscopically and the implantation time ranged from two to 20 minutes.
Primary post-operative endpoints were recorded at hospital discharge; at one, three and six weeks; at three, six and 18 months; and at three years. These endpoints included pain relief over time, and changes in range of motion, activities of daily living and shoulder strength measured with the Constant score. Complications and device-related adverse events were also recorded.

**Effectiveness**

Three patients did not reach the three-year follow-up. One patient withdrew consent six weeks after implantation due to an unsatisfactory outcome and was referred to reverse total shoulder arthroplasty. The second patient had improvement in symptoms but refused to continue to participate in the study, while the third patient died during follow-up from cardiac disease unrelated to the implantation.

Statistically significant improvements occurred in all parameters measured, including subjective pain score, night pain, total Constant score, activities of daily living, range of motion and shoulder power. The times at which significant improvement occurred are reported in Table 2. For all measurable parameters, once an improvement reached statistical significance ($p>0.05$), it was maintained throughout the follow-up period.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time after implantation when statistically significant improvement occurred</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective pain score</td>
<td>1 week</td>
<td>$p=0.0021$</td>
</tr>
<tr>
<td>Night pain</td>
<td>1 week</td>
<td>$p&lt;0.0001$</td>
</tr>
<tr>
<td>Total Constant score</td>
<td>6 weeks</td>
<td>$p=0.010$</td>
</tr>
<tr>
<td>Activities of daily living</td>
<td>3 weeks</td>
<td>NR</td>
</tr>
<tr>
<td>Range of motion</td>
<td>6 weeks</td>
<td>NR</td>
</tr>
<tr>
<td>Shoulder power</td>
<td>1.5 years</td>
<td>$p=0.0003$</td>
</tr>
</tbody>
</table>

NR, not reported

**Safety**

It was suspected that two patients who showed no improvement in their Constant scores had non-clinically significant synovitis (inflammation of the membrane that lines the shoulder joint). Post-surgery imaging did not reveal any bone cysts or significant synovitis in any of the evaluated patients. No other device- or procedure-related adverse events were noted during the follow-up period.
A conference abstract reported on a prospective, on-going case series of patients (total number not stated) implanted with the InSpace biodegradable subacromial spacer balloon (level IV interventional evidence). The study discussed the results from the first 22 of 35 balloons implanted (21 patients in total as one patient had both shoulders operated on), with a mean follow-up of 24 months. All patients had massive irreparable rotator cuff tears. It is not stated whether they were consecutive.

**Effectiveness**

Good or excellent results were reported in 86 per cent of patients, with complete pain relief and a very rapid recovery (often after six weeks) of active and painless range of motion. The mean Constant score improved and almost doubled post-operatively (no statistical analyses were provided). The improvement in shoulder power continued up to 18 months after implantation. Losses to follow-up were not reported.

**Safety**

Not reported.

**Economic evaluation**

No economic evaluation studies on the InSpace biodegradable subacromial spacer were identified. Similarly, no data on the cost of shoulder hemiarthroplasty, arthroplasty or on the different rotator cuff repair procedures that could be used in a comparative economic evaluation were identified.

**Ongoing research**

Six ongoing trials involving the InSpace biodegradable subacromial spacer, all of which are industry-sponsored, were identified from a search of ClinicalTrials.gov and the Australian New Zealand Clinical Trials Registry (Table 3).
<table>
<thead>
<tr>
<th>Trial Identifier</th>
<th>Location</th>
<th>Trial status</th>
<th>Study design</th>
<th>Intervention</th>
<th>Selection criteria</th>
<th>Primary outcome</th>
<th>Estimated completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02210910</td>
<td>Israel</td>
<td>Recruiting</td>
<td>RCT Single centre n=40</td>
<td>InSpace or best surgical repair</td>
<td>Positive MRI of affected shoulder indicating full-thickness, large to massive rotator cuff tear &gt;3cm in diameter involving one or more tendons; pain and disability ≥3 months.</td>
<td>Change in shoulder score</td>
<td>December 2016</td>
</tr>
<tr>
<td>NCT02208440</td>
<td>United Kingdom</td>
<td>Recruiting</td>
<td>RCT Single centre n=40</td>
<td>InSpace or best surgical repair</td>
<td>Positive MRI or CT of affected shoulder indicating full-thickness, massive rotator cuff tear ≥5cm in diameter or long, narrow tears ≥4cm² including fatty infiltration grade III or IV involving more than one tendon; pain and disability ≥3 months.</td>
<td>Change in shoulder score</td>
<td>July 2016</td>
</tr>
<tr>
<td>NCT02211183</td>
<td>Spain</td>
<td>Recruiting</td>
<td>RCT Single centre n=40</td>
<td>InSpace or best surgical repair</td>
<td>Positive MRI or CT of affected shoulder indicating full-thickness, massive rotator cuff tear ≥5cm in diameter or long, narrow tears ≥4cm² including fatty infiltration grade III or IV involving more than one tendon; pain and disability ≥3 months.</td>
<td>Change in shoulder score</td>
<td>December 2016</td>
</tr>
<tr>
<td>NCT01890733</td>
<td>Italy</td>
<td>Recruiting</td>
<td>RCT Single centre n=40</td>
<td>InSpace or best surgical repair</td>
<td>Positive MRI or CT of affected shoulder indicating full-thickness, massive rotator cuff tear ≥5cm in diameter or long, narrow tears ≥4cm² including fatty infiltration grade III or IV involving more than one tendon; pain and disability ≥3 months.</td>
<td>Change in shoulder score</td>
<td>December 2015</td>
</tr>
<tr>
<td>NCT02208453</td>
<td>Italy</td>
<td>Recruiting</td>
<td>Case series Single centre n=15</td>
<td>InSpace</td>
<td>Positive MRI or CT of affected shoulder indicating full-thickness, massive rotator cuff tear ≥5cm in diameter or long, narrow tears ≥4cm² including fatty infiltration grade III or IV involving more than one tendon; pain and disability ≥3 months.</td>
<td>Change in shoulder score</td>
<td>March 2016</td>
</tr>
<tr>
<td>NCT00916994</td>
<td>Israel</td>
<td>Ongoing, not recruiting</td>
<td>Case series Multicentre n=70</td>
<td>InSpace</td>
<td>X-ray of shoulder with no unrelated pathology and imaging (ultrasound or MRI) showing rotator cuff tear; pain and disability ≥4 months; failure of conservative treatment; normal blood cell counts and liver function; negative for HIV, hepatitis B or C and not pregnant.</td>
<td>Serious adverse event rate</td>
<td>December 2014</td>
</tr>
</tbody>
</table>

CT, computed tomography; HIV, human immunodeficiency virus; MRI, magnetic resonance imaging; RCT, randomised controlled trial

InSpace biodegradable subacromial spacer: March 2015
Other issues

In support of their research or manuscript preparation, one or more of the authors of the study by Senekovic et al (2013) received grants or outside funding from Ortho-Space Ltd. In addition, Ortho-Space Ltd paid or directed, or agreed to pay or direct, benefits to a research fund, foundation, educational institution or other charitable or non-profit organisation with which the authors were affiliated or associated. Two of the study authors had a financial interest in Ortho-Space Ltd.

The authors of the study by Senekovic et al 2013 noted several weaknesses with their study. They stated that the shoulder functional assessment was based solely on the Constant score, which might be limited in its scope and can be gender biased in regard to power measures. In addition, the lack of an established protocol for radiographic evaluation modalities made the comparison between pre- and post-treatment imaging impossible. The lack of a control group also weakened the results.

Summary of findings

Evidence on the use of the InSpace biodegradable subacromial spacer was only available from two case series studies, one in the form of a conference abstract. All patients had massive, irreparable rotator cuff tears. Both studies reported improvements in mean range of motion and Constant score (a measure of shoulder function). Other parameters that were assessed in one of the studies included subjective pain score, night pain, activities of daily living and shoulder power. All parameters significantly improved during the post-operative period, and once the improvement reached statistical significance ($p>0.05$) it was sustained throughout the follow-up period. Both studies reported continued improvement in patients well beyond the time at which the balloon was expected to degrade. No serious complications or adverse events occurred in the single study that reported safety outcomes.

HealthPACT assessment

Although positive results were reported in this assessment, the evidence-base supporting the use of the InSpace device is limited, as reflected in the current lack of TGA marketing approval. However, it is likely this device will have greater uptake in the private rather than the public hospital sector; therefore it is recommended that no further research on behalf of HealthPACT is warranted at this time.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT website.

Total number of studies 2
Total number of Level IV studies: 2

**Search criteria to be used (MeSH terms)**

InSpace OR subacromial spacer OR subacromial biodegradable spacer OR biodegradable spacer OR balloons spacer AND rotator cuff surgery OR rotator cuff injury

**References**


shoulder and elbow surgery / American Shoulder and Elbow Surgeons [et al], 20 (1), 146-57.


