Health Policy Advisory Committee on Technology

Technology Brief

BioZorb™ Tissue Marker

August 2016

ASERNIP-S

Australian Safety and Efficacy Register of New Interventional Procedures – Surgical

Royal Australasian College of Surgeons

HealthPACT

emerging health technology

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This Brief was commissioned by Queensland Health, in its role as the Secretariat of the Health Policy Advisory Committee on Technology (HealthPACT). The production of this Brief was overseen by HealthPACT. HealthPACT comprises representatives from health departments in all States and Territories, the Australian and New Zealand governments and MSAC. It is a sub-committee of the Australian Health Ministers' Advisory Council (AHMAC), reporting to AHMAC's Hospitals Principal Committee (HPC). AHMAC supports HealthPACT through funding.

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Summary of findings

The BioZorb™ marker was developed to provide three-dimensional delineation of the surgical site after breast tumour removal. The surgeon implants the device during lumpectomy so that the radiation oncologist can later see the volume and location of the removed tumour. This can have major implications for the accuracy of boost phase radiation therapy, potentially reducing treatment time. An additional benefit is that BioZorb can help maintain the previous shape of the breast, resulting in better cosmetic outcomes.

Evidence for the safety and efficacy of Biozorb is poor and limited to conference abstracts. Findings from the conference abstracts (N = 277) reporting on five case series studies performed in the United States of America and New Zealand suggested that the device is easy to visualise by radiation oncologists, does not require new surgical techniques to implant, and maintains the shape of the breast. The maximum follow-up was three years, involving x-ray (mammography) and ultrasound imaging. It was found to be more effective as tissue treatment volume was decreased and treatment protocol accelerated when compared with standard targeting methods, resulting in a reduced need for conventional radiotherapy sessions. Safety issues were not specifically identified; however, the studies are very recent and longer-term results are needed to capture any safety issues. Economic information is provided by two studies which conducted cost analyses, both showing a cost reduction due to treatment efficiencies. No Australia-specific economic information is available.

HealthPACT Advice

Markers such as the BioZorb™ are intended to assist in the post-surgical visualisation of the tumour site and in so doing assist in the planning and patient positioning during follow-up radiotherapy treatment. There appears to be little evidence to support an advantage in patient outcomes or in health system savings with the use of the BioZorb™. Therefore, HealthPACT does not support public investment in the BioZorb™ tissue marker system in clinical practice, and recommends no further review of the evidence is warranted at this time.

Technology, Company and Licensing

Register ID	**WP236**
Technology name	**BioZorb™**
Patient indication	**Women with breast cancer undergoing lumpectomy during breast conservation surgery.**

Description of the technology

The BioZorb™ marker is a bioabsorbable polylacticacid (thermoplastic polyester derived from renewable resources such as corn starch or sugarcane) helix tissue marker used for radiographic marking of soft tissue sites such as breast lumpectomies (also called breast conserving surgery, partial mastectomy or wide excision). It is sutured into the cavity following surgical removal of cancerous breast tissue.[1] The bioabsorbable spiral has six titanium marker clips that enable radiation oncologists to visualise in 3D the tumour site and size after surgery. Thus, the marker assists in targeting for radiotherapy treatment planning and patient positioning during radiotherapy treatment, and it has the ability to facilitate advanced methods of radiotherapy treatment.[2] It comes in several sizes and can be used in conjunction with surgical breast reconstruction (oncoplastic) techniques.[3] BioZorb is compatible with a variety of image-based tracking methods. The spiral is reabsorbed by the body in a year or more, while the marker clips remain.[4]

Eligible patients include women with early stage—stage I or II—breast cancer who are able to undergo breast conserving surgery.[2] The BioZorb marker is contraindicated in patients with more than one breast tumour (multifocal disease), breast implants, serious medical conditions[5] and comorbid medical issues such as diabetes or being a smoker.[6]

Figure 1 BioZorb device (image printed with permission)[7]

Company or developer

Focal Therapeutics, California, Unites States of America.

Reason for assessment

The BioZorb marker may have considerable clinical and cost saving benefits. Clinicians experience ongoing difficulties in precisely identifying the area of tumour resection in patients following breast cancer surgery. Currently, there is no standardised method of providing a visual cue for monitoring the tumour bed site during post-operative treatment and surveillance. This may lead to treatment of a larger than necessary breast volume, with resultant complications, and also potentially limits the use of advanced radiation therapy technologies such as three-dimensional conformal and intensity-modulated radiation therapy.[8]

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 BioZorb marker received 510(k) clearance from the United States Food and Drug Administration in February 2012. It is indicated for radiographic marking of sites in soft tissue and was determined to be not dissimilar to vascular clips as the predicate device.[9]

Published advertising and personal communication with the manufacturer confirmed that the manufacturer is currently working toward CE Mark approval of the device within the next two years.[7, 10]

Australian Therapeutic Goods Administration approval

- ☐ Yes — ARTG number (s): Not applicable
- ☒ No
- ☐ Not applicable

Technology type **Device**

Technology use **Therapeutic/Diagnostic (assists in delineating radiotherapy site)**

Patient Indication and Setting

Disease description and associated mortality and morbidity

When the development of breast cancer is hormone-related, risk factors differ for this cancer in post-menopausal (most commonly diagnosed) and pre-menopausal women.[11] Types of breast cancer are divided into invasive and non-invasive.

Non-invasive breast cancer, called carcinoma in situ, is found in the milk ducts and does not spread outside the breast. Invasive breast cancer has the ability to spread outside the breast and accounts for around 80 per cent of breast cancers. Other less common types of breast cancer include invasive lobular breast cancer, inflammatory breast cancer and Paget's disease of the breast. Secondary or metastatic breast cancer occurs when breast cancer spreads to other parts of the body, usually through the lymph nodes and/or the bloodstream.[12, 13]

Mortality and morbidity

Approximately one in eight Australian women are diagnosed with breast cancer during their lifetime, with the majority diagnosed between 50 and 69 years of age. Breast cancer is the most common cancer (28% of all cancers) in Australian women (including Aboriginal and Torres Strait Islander women) and the second most common cancer to cause death in women after lung cancer. Approximately 14,000 women and 130 men (who make up less than 1% of all breast cancers) are diagnosed with breast cancer each year.[14] In 2014 there were 2,814 female deaths under the principal diagnosis of malignant neoplasm of the breast. It was the sixth most common cause of death for women in Australia.[15]

Breast cancer is New Zealand's third most common cancer and it accounts for more than 600 deaths each year.[16] The average annual rate of new cases of breast cancer was 94 per 100,000 women in the period 2008 to 2012. During the same time period, the average rate of death from breast cancer was 19 per 100,000 women per year.[17]

Most people with early breast cancer can be treated successfully, due to better diagnostic tests and scans, earlier detection and improvements in treatment methods. According to recent statistics, the five-year survival rate for Australian women with invasive ductal carcinoma is 90 per cent.[14] The 5-year cumulative incidence of metastatic breast cancer for women originally diagnosed with non-metastatic breast cancer is five to 18 per cent. [18]

Number of patients

In the Australian public hospital system between 2013 and 2014 there were 25,367 separations reported under the principal diagnosis of malignant neoplasm of the breast.[19] During the same time period, 21,464 patients in the Australian public hospital system underwent excision of lesion of breast (an unknown portion of these procedures were

lumpectomies) and 425 excisions of accessory breast tissue (an unknown portion of these procedures were lumpectomies).[20]

In the New Zealand public hospital system between 2012 and 2013 there were 3,285 discharges reported for malignant neoplasm of the breast. During the same period, 755 patients in the New Zealand public hospital system underwent excision of lesion of breast (an unknown portion of these procedures were lumpectomies) and 93 other excision procedures on breast (an unknown portion of these procedures were also lumpectomies).[21]

Speciality	**Surgical oncology and radiotherapy**
Technology setting	**Specialist/General Hospital**

Impact

Alternative and/or complementary technology

Additive and substitution: The BioZorb marker can be used as a substitute for vascular clips and seroma activity, but may also be used in combination with these techniques.

Current technology

Breast cancer is treated using a combination of surgery, chemotherapy and radiation therapy. Surgery is usually the first treatment, often followed by a combination of chemotherapy, radiation therapy, hormone or biological treatments. The type of surgery and treatment plan depends on the type of cancer and includes:

- Lumpectomy—removal of the cancerous lump along with a small rim of normal tissue around it
- Total mastectomy—removal of the whole breast
- Radical mastectomy—removal of the breast, most of the lymph nodes under the arm, and often the lining over the chest muscles.[11]

In many cases, breast surgery involves oncoplastic techniques, where surgeons try to reduce the cosmetic deformity caused by the tissue removal.[22]

Radiation treatment is administered using various methods. These include whole breast radiation with boost phase radiation therapy (conventional or accelerated fractionation protocol) or partial breast radiation (interstitial brachytherapy, multiple field image-guided radiation therapy or Intensity-modulated radiation therapy).[23] Ease of visibility of the tumour site is important for radiation oncologists.[5]

Current methods for targeting tissue for radiation treatment after surgery include the use of anatomic landmarks, radio-opaque clips placed during surgery and the presence of seroma (a fluid that builds up under the skin after surgery) on a computed tomography (CT) scan. However, radio-opaque clips cannot define a volume, are difficult to differentiate from vascular clips and can migrate away from the tumour site.

Seroma is also problematic because it can spread into surrounding glandular tissue or may not even be present when the surgical site is closed using oncoplastic techniques. Consequently, these methods can lead to an overestimation of breast treatment volume and inappropriate exposure of healthy tissue to radiation. These techniques may also fall short of the precision needed for newer methods of radiotherapy delivery.[8]

Diffusion of technology in Australia

Currently unavailable.

International utilisation

The BioZorb marker is currently distributed and in clinical use in the United States of America and New Zealand.[24] It is not known how many women have been implanted with the BioZorb marker.

Country	Level of Use		
	Trials underway or completed	Limited use	Widely diffused
USA	✓	✓	
New Zealand	✓	✓	

Cost infrastructure and economic consequences

The listed price of the device in the United States of America is $1,728.45[a].

Ethical, cultural, access or religious considerations

No ethical, cultural, access or religious considerations were identified that may limit the use of this technology.

a AUD = 0.720 USD, currency conversion performed on 12 May 2016, source XE Currency Converter

Evidence and Policy

Safety and effectiveness

Evidence assessed in this Brief comes from five conference abstracts based on case series (level IV interventional evidence) studies. While other abstracts were available, this Brief included only the most relevant and recent on the use of BioZorb for targeting breast tissue for radiation therapy after surgery. An overview of the studies is provided in Table 1.

Table 1 Included study characteristics

Study details	Design	Location	Participants	Follow-up
Cross et al 2015[25]	Case series	USA	109	36 months
Cross et al 2014b[3]	Case series	USA	65	NR
Smith et al 2014[26]	Case series	USA New Zealand	51	12 months
Cross et al 2013a[8]	Case series	USA	36	NR
Harman et al 2013[27]	Case series	New Zealand	16	16 months

NR: not reported, USA = United States of America

Safety

Safety outcomes were not quantified in any of the included studies. Five broadly reported that there were no complications related to the device,[3, 8, 26-28] while the remaining study did not report on safety.

Effectiveness

Cross et al 2015[25]

The BioZorb marker was implanted in 109 women during partial mastectomy, enrolment method not described. Each patient's case was discussed at multidisciplinary tumour board meetings. Decisions regarding radiation regimens were optimised for each patient: 37 per cent of patients received conventional full-course whole breast irradiation plus boost; 57 per cent received hypo-fractionation plus boost; and 4 per cent received accelerated partial breast irradiation. In 96 per cent of cases the marker was found (as assessed by a non-validated tool) to be "useful" during radiation treatment planning for target delineation. Over three years of routine use of the implant there was a marked increase in the use of hypo-fractionated (shorter) radiation regimens to 90 per cent of cases. The patients were followed-up for 36 months. There is potential overlap between this study and the other included studies; potential overlap is outlined in Table 2.

Cross et al 2014b[3]

The BioZorb marker was implanted in 65 women during partial mastectomy, enrolment method not described. Post-operative treatment plans for radiation or chemotherapy were completed. It was demonstrated that incorporating oncoplastic techniques while implanting the device improved treatment and cosmetic outcomes, but the measure used to assess this was not reported. The treatment volume was decreased by 50 per cent when compared with standard targeting methods. In patients for whom the marker facilitated an accelerated protocol, total radiotherapy treatment time decreased to between 5 to 7 days compared with standard treatment time (the standard treatment time was not stated).

Smith et al 2014[26]

The BioZorb marker was implanted in 51 women during lumpectomy; however, the enrolment method was not described. All markers were retained without migration or extrusion. On average planned treatment volumes were reduced by 55 per cent, reducing the number of brachytherapy catheters by 47 per cent (method of comparison not reported). Standard deviations were not reported. When planning, the marker was rated as "useful" in 90 per cent of cases and "not/somewhat useful" in 10 per cent of cases.

Cross et al 2013a[8]

The BioZorb marker was implanted in 36 consecutive patients during partial mastectomy. It is unclear whether these patients were included in the 109 patients in Cross et al 2015. Post-operative CT scans and treatment plans were generated and compared. The tissue marker was rated for its utility in defining the target area for treatment planning as well as day-to-day positioning of patients between fractions.

Of the 36 patients, 25 (69%) completed adjuvant radiotherapy. Where specifically tracked, it was found that the utility of the marker was rated (by a non-validated tool) to be very useful for boost planning in 80 per cent of cases. Moreover, the increased accuracy enabled by the BioZorb marker led the radiation oncology team to employ advanced and accelerated treatment methods in 14 per cent of patients. In a subgroup of five patients where cavity volumes were compared with and without three-dimensional marker guidance, marker guidance led to a 47 per cent reduction in planned cavity treatment volume.

Harman et al 2013[27]

The BioZorb marker was implanted in 16 consecutive patients during partial mastectomy. Multiple treatment plans were generated and compared. When compared to conventional methods of determining the target area, use of the marker resulted in treatment volumes that were reduced by >60 per cent. In 'appropriate patients' (definition not provided) the marker also facilitated the use of an accelerated protocol, decreasing total treatment time from 6 weeks to 5 days.

An indication of potential study overlap among authors is provided in Table 2. It should also be noted that Dr Lebovic, a co-author of Cross et al (2014b), serves as the Chief Medical Officer for Focal Therapeutics.

Table 2 Author overlap among the included studies

Authors	Year	Participants	Institutions
Cross, M. Ross, J. Jones, S. Smith, A. Beck, T.	2015[25]	109	• Highlands Oncology Group, Rogers, Arkansas, USA • Breast Treatment Associates, Fayetteville, Arkansas, USA
Cross, M. Ross, J. Jones, S. Beck, T. Schonholz, S. Kaufman, C. S. Lebovic, G.	2014b[3]	65	• Breast Treatment Associates, Fayetteville, Arkansas, USA • Highlands Oncology Group, Fayetteville, Arkansas, USA • Noble Hospital, Westfield, Massachusetts, USA • Bellingham Breast Center, Bellingham, Washington, USA • American Society of Breast Disease, Frisco, Texas, USA
Smith, L.A. Kuske, R. R. Cross, M.	2014[26]	51	• Comprehensive Breast Care, Albuquerque, New Mexico, USA • Arizona Breast Cancer Specialists, Scottsdale, Arizona, USA
Cross, M. Ross, J. Jones, S. Beck, T.	2013a[8]	36	• Breast Treatment Associates, Fayetteville, Arkansas, USA • Highlands Oncology Group, Rogers, Arkansas, USA

USA: United States of America.

Qualitative results

It was qualitatively reported that the marker was easily and consistently visualised and was easy to use with standard surgical techniques.[3, 8, 25-27] The cosmetic result was described as "excellent"[3, 8, 27] in three studies and "good to excellent" in one.[28]

Economic evaluation

A study by Cross et al[25] conducted a cost analysis by collecting available information on radiation therapy in 46 patients. It was reported that increased confidence in targeting enabled more frequent use of field-in-field planning to improve dose homogeneity in in accelerated radiation therapy regimens. The shift from conventional whole breast radiotherapy (average cost $35,369) to hypo-fractionated radiotherapy (average cost

$26,323) was driven by the higher confidence in targeting due to the presence of the BioZorb marker. The average decrease in treatment costs was 25 per cent ($9,040)[b].

Harman et al[27] reported that the BioZorb device resulted in improvements in clinical imaging and radiation treatment planning and delivery, enabling the use of accelerated techniques for delivery of radiotherapy. The reduced number of dose fractions meant fewer daily visits and faster completion of treatment (e.g. 6 weeks to 5 days) for patients. This translated into lower costs for the delivery of breast cancer radiotherapy ($6,925 versus $13,850), but the method of cost analysis was not described[c].

Ongoing research

In searches of ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Registry, no ongoing clinical trials on surgical coaching were identified.

Other issues

No publications from peer-reviewed sources were identified on Biozorb. The evidence relies upon conference abstracts.

Three of the conference abstracts included in this Brief were sourced from the BioZorb manufacturer's website.[3, 8, 26]

A newer tissue marker device, BioZorb LP, has been produced by Focal Therapeutics. This smaller, "low profile" design will allow the marker to be used in women with small breasts, tumours in superficial cavities or locations with minimal tissue.[29]

An Australia study has been published comparing the use a clip-based protocol (min 4) with no clips for visibility and volume during radiotherapy, using a non-concurrent control. The clips improved localisation of the surgical site for radiotherapy targeting but did not reliably improve volume. This protocol is currently being used in the Northern Sydney Cancer Centre in Australia.[30]

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 web site.

Total number of studies:	6
Total number of level IV (case series) studies:	5

Search criteria to be used (MeSH terms)

Date searched: 18/03/2016

b AUD = 0.739 USD, currency conversion performed on 11 May 2016, source XE Currency Converter
c AUD = 1.081 NZD, currency conversion performed on 11 May 2016, source XE Currency Converter

Search terms:

1) BioZorb
2) Implantable marker OR implantable tissue marker AND breast
3) Three/3 dimensional marker OR three/3 dimensional tissue marker OR three/3 dimensional volumetric marker AND breast
4) Bioabsorbable lumpectomy marker
5) 1 OR 2 OR 3 OR 4

References

1. Valerio, M., Ahmed, H. U. et al (2014). 'The role of focal therapy in the management of localised prostate cancer: a systematic review'. *European Urology*, 66 (4), 732-51.
2. Glaser, C. C., Cross, M. J.& Harman, J. A new method for marking the lumpectomy cavity during oncoplastic surgery and breast conservation. 36th Annual CTRC AACR San Antonio Breast Cancer Symposium; December 10-14, 2013; San Antonio, TX2013.
3. Cross, M., Ross, J. et al. Identifying the Surgical Cavity after Oncoplastic Breast Surgery. ASCO 2014 Breast Cancer Symposium; September 4-6, 2014; San Francisco, CA2014b.
4. Kaufman, C. S., Hall, W. et al. Initial experience with novel 3d bioabsorbable lumpectomy marker. 16th Annual Meeting of the American Society of Breast Surgeons; April 29 -May 3, 2015; Orlando, FL2015a. p. 67.
5. Cross, M., Ross, J. et al. Use of a 3-D Bioabsorbable Tissue Marker to Delineate the Lumpectomy Cavity for Radiation Treatment Planning. 14th Annual Meeting of the American Society of Breast Surgeons; May 1-5, 2013; Chicago, IL2013b.
6. Cross, M., Ross, J. et al. Benefits of a 3-D Volumetric Marker for Delineating the Tumor Bed. Presented at 2014 World Congress on Breast Healthcare; October 16-19, 2014; Orlando, FL2014a.
7. Plagakis, S., O'Callaghan, M. et al (2015). 'Surgical pathology outcomes for discontinued active surveillance in South Australian men with prostate cancer'. *BJU International*, 115, 7.
8. Cross, M., Ross, J. et al. Utility of a three-dimensional bioabsorbable tissue marker in delineating the lumpectomy cavity. ASCO Breast Cancer Symposium; September 7-9, 2012; San Francisco, CA2013a.
9. Food and Drug Administration (2012). *510(k) summary*. [Internet]. Food and Drug Administration,. Available from: http://www.accessdata.fda.gov/cdrh_docs/pdf11/k113202.pdf [Accessed 17th May 2016].
10. Life Science Intelligence (2014). *Emerging Medical Technologies (EMT)® Innovator of the Month*. [Internet]. Life Science Intelligence,. Available from: http://focalrx.com/wp-content/uploads/2014/01/LSI-Innovator-of-the-Month-Feb-2014.pdf [Accessed 17th May 2016].
11. World Cancer Reseaech Fund (2015). *Breast cancer statistics*. [Internet]. Continuous Update Project. Available from: http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/breast-cancer-statistics [Accessed 10th May 2016].

12. NHS Choices *Breast cancer (female)*. [Internet]. NHS. Available from: http://www.nhs.uk/Conditions/Cancer-of-the-breast-female/Pages/Introduction.aspx [Accessed 10th May 2016].
13. Breast Cancer Care WA (2013). *What is breast cancer?* [Internet]. Breast Cancer Care WA. Available from: http://www.breastcancer.org.au/about-breast-cancer/what-is-breast-cancer.aspx?gclid=CLidlbfizswCFc4AvAod2D8Plg [Accessed 10th May 2016].
14. Cancer Council Australia (2016). *Breast Cancer*. [Internet]. Cancer Council Australia. Available from: http://www.cancer.org.au/about-cancer/types-of-cancer/breast-cancer.html#note_1 [Accessed 12th May 2016].
15. Australian Bureau of Statistics (2016). *3303.0 - Causes of death, Australia, 2014*. [Internet]. Australian Bureau of Statistics. Available from: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/3303.0~2014~Main%20Features~Leading%20Causes%20of%20Death%20by%20Sex~10036 [Accessed
16. Ministry of Health (2015). *Breast Cancer*. [Internet]. Ministry of Health. Available from: http://www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/breast-cancer [Accessed 11th May 2016].
17. Ministry of Health (2015). *Cancer: Historical summary 1948–2012*. [Internet]. Ministry of Health. Available from: http://www.health.govt.nz/publication/cancer-historical-summary-1948-2012 [Accessed 11th May 2016].
18. Lord, S. J., Marinovich, M. L. et al (2012). 'Incidence of metastatic breast cancer in an Australian population-based cohort of women with non-metastatic breast cancer at diagnosis'. *Med J Aust*, 196 (11), 688-92.
19. Australian Institute of Health and Welfare (2014). *Separation statistics by principal diagnosis (ICD-10-AM 8th edition) Australia, 2013-2014*. [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/hospitals-data/principal-diagnosis-data-cubes/ [Accessed 5th May 2016].
20. Australian Institute of Health and Welfare (2014). *Procedures and healthcare interventions (ACHI 8th edition), Australia, 2013-2014.* [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/hospitals-data/procedures-data-cubes/ [Accessed 5th May 2016].
21. Ministry of Health (2015). *Pivot tables - publicly funded hospital discharges 2012 to 2013*. [Internet]. Ministry of Health. Available from: http://www.health.govt.nz/system/files/documents/publications/pubdischargesprocedures2012-13_pivotfinal_0.xlsb [Accessed 12th May 2016].
22. MedlinePlus (2016). *Mastectomy*. [Internet]. US Department of Health and Human Services. Available from: https://www.nlm.nih.gov/medlineplus/mastectomy.html [Accessed 11th May 2016].
23. Kuske, R. R., Cross, M. et al. Utility of a Novel 3-D Marker in Treatment Planning for Breast Cancer. American Society of Radiation Oncology annual meeting; September 22-25, 2013; Atlanta, GA2013.
24. Chang Clark, J. (2015). *Medgadget Interview With Focal Therapeutics: The Latest Data on BioZorb and Its Potential*. [Internet]. Med Gadget. Available from: http://www.medgadget.com/2015/08/medgadget-interview-focal-therapeutics-latest-data-biozorb-potential.html [Accessed 17th May 2016].
25. Cross, M., Ross, J. et al. Implantable marker to facilitate use of hypofractionated radiation in early breast cancer. Breast Cancer Symposium 2015; September 25-27, 2015; San Francisco, CA2015.

26. Smith, L. A., Kuske, R. R.& Cross, M. Improved Targeting of the Lumpectomy Cavity Using a Spiral 3-D Marker. American Society of Radiation Oncology 56th Annual Meeting; September 14-17, 2014; San Francisco, CA2014.
27. Harman, J., Govender, S. et al. An improved method for marking the surgical cavity during partial mastectomy. 64th Annual Scientific Meeting of the Royal Australian and New Zealand College of Radiologists, RANZCR 2013 October 17-20, 2013; Auckland, New Zealand2013. p. 137.
28. Kaufman, C. S., Hall, W. H. et al. Clinical use of a three-dimensional tissue marker to target postlumpectomy radiation. Breast Cancer Symposium 2015; San Francisco, CA2015b.
29. Laidley, A. (2016). *Dr Alison Laidley and BioZorb LP* Available from: https://www.youtube.com/watch?v=QEjRuAzuVuQ [Accessed 27 May 2016].
30. Lewis, L., Cox, J. et al (2015). 'A clip-based protocol for breast boost radiotherapy provides clear target visualisation and demonstrates significant volume reduction over time'. *J Med Radiat Sci*, 62 (3), 177-83.