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Dear Dr Forstner

This is a joint submission from the Breast Cancer Network Australia (BCNA) and the Breast Cancer Aotearoa Coalition (BCAC) that provides feedback on the draft Faculty of Radiation Oncology Position Paper on Techniques and Technologies in Radiation Oncology 2015 Horizon Scan for Australia and New Zealand. We write jointly to the RANZCR to suggest that the Faculty amend its position that Intra-Operative Radiation Therapy (IORT) is not supported by sufficient evidence to form a view.

We note that the beneficial outcomes of IORT extend beyond its ability to prevent the local recurrence of breast cancer. Fewer side effects and the ability of women to complete breast cancer treatment earlier are significant factors for patients. Additionally, provision of easy access to an effective treatment for rural women and Indigenous women, particularly Māori and Aboriginal and Torres Strait Islander women, whose access and outcomes are currently worse, should be considered and given due weight by RANZCR in reaching its view.

About Breast Cancer Network Australia

Breast Cancer Network Australia (BCNA) is the peak national organisation for Australians personally affected by breast cancer. BCNA supports, informs, represents and connects people whose lives have been affected by breast cancer. BCNA works to ensure that Australians affected by breast cancer receive the very best support, information, treatment and care appropriate to their individual needs.

BCNA represents more than 110,000 individual members and 300 member groups from across Australia.

About BCAC

The Breast Cancer Aotearoa Coalition (BCAC) is a broadly representative incorporated charitable society established in 2004 to provide a unified, evidence-based voice for the New Zealanders affected by breast cancer. Our membership comprises more than 30 breast cancer-related groups from around New Zealand, as well as many individual members.

BCAC is run by a committee of women who have experienced breast cancer. We work as volunteers to make world class detection, treatment and care accessible to all those affected by breast cancer in New Zealand. By virtue of our experience and knowledge of this disease, as well as our networks across breast cancer patients, groups and clinicians around the country we are able to provide valuable insights into improvements that can be made in the provision of breast cancer services.

Together BCNA and BCAC represent a wide spectrum of breast cancer patients and organisations across Australia and New Zealand.

Evidence for intra operative radiation therapy

In relation to the level of evidence available for IORT, we note that the Faculty references the 2010 ASTRO Emerging Technology Committee Report that concluded that at that time “...any advantages of electronic brachytherapy device (EBT) are as yet unproven in terms of efficacy or patient outcomes. However, there are potential therapeutic advantages inherent in the low energy EBT device compared to HDR sources, warranting further investigation”. We maintain that this view is outdated given the evidence provided more recently in Vaidya *et al.* 2010, 2014 and in the supporting data provided from the TARGIT-A trial that used the Intrabeam device.

We support Vaidya *et al.*'s (2014) interpretation of the 5 year results for local recurrence and first analysis of overall survival from this trial that “*TARGIT concurrent with lumpectomy within a risk-adapted approach should be considered as an option for eligible patients with breast cancer carefully selected as per the TARGIT-A trial protocol, as an alternative to postoperative external beam radiation therapy (EBRT)*”.

BCNA and BCAC are concerned that the view expressed in the Faculty's draft position paper may serve to slow the introduction of this treatment in both our countries and that this will deprive women of an important treatment option. Targeted IORT (Intrabeam) offers several significant clinical benefits to patients and we believe that this radiotherapy option should be offered to patients who meet the TARGIT criteria and who have been fully informed of potential risks and benefits. As with other breast cancer treatments, eligible patients should be given all the relevant information in an accessible format so they can weigh their options and make the best treatment decision for themselves.

External beam radiation therapy: the woman's perspective

Women who have had a lumpectomy for low risk breast cancer will usually be offered adjuvant EBRT 5 to 12 weeks after surgery. The additional burden of 3 to 6 weeks of radiotherapy can have a significant impact on a woman's quality of life, the course of her treatment, and her overall health and wellbeing.

Women often report challenges with EBRT, including:

- Difficulties accessing radiotherapy. Women who need to travel long distances to receive radiotherapy may experience personal and financial hardship. Treatment decisions may be made based on their geographical living arrangements. Such women may choose not to access radiotherapy and suffer poorer outcomes as a consequence.
- The side effects of radiotherapy. Women will often experience skin reactions, which can be distressing and painful. Fatigue is also a very common side effect of radiotherapy, which can impact on a woman's quality of life.

Accessing external beam radiotherapy

The usual course of radiotherapy for women with breast cancer involves 3 to 6 weeks of daily treatment. Though the procedure itself may take minutes, the travel, waiting time, and the time spent away from family and/or work has an adverse impact on many women and their families.

Women living in rural and remote areas are particularly disadvantaged by the requirements of EBRT. Distance from a radiotherapy centre has been shown to be associated with reduced uptake of EBRT¹. In a US study, non-completion was associated with higher rates of local recurrence².

In Australia, Indigenous Australians living in remote areas have significantly lower survival than their non-Indigenous counterparts³. Indigenous Australians are likely to receive less active treatment for cancer than non-Indigenous Australians. The reasons for lower treatment rates are not clear; however travel and distance are known barriers to optimal care.

In New Zealand, rural and Māori women have been shown to have slower and reduced access to breast cancer treatments including radiotherapy and this is associated with poorer breast cancer outcomes⁴. Introduction of IORT could improve treatment access and survival outcomes for Indigenous women in Australian and New Zealand, thus helping to address inequities in care. This is of particular importance and urgency for Maori women who have the highest incidence of breast cancer of any indigenous population in the world^{5 6} and whose rate of survival from breast cancer is consistently and significantly lower than for other ethnicities in New Zealand^{7 8 9}.

Rural and remote women are often required to attend a major regional centre or city to have radiotherapy and may need to spend up to six weeks away from home as a result. The financial burden of 3 to 6 weeks without an income stream or home-based support for their families, particularly with Patient Travel Assistance Schemes providing limited relief, is particularly onerous for women who may have already taken significant amounts of time away from work for breast cancer treatment. Travel commitments may also have an impact on partners/carers who may also be required to take extended time from work, placing even greater strain on family budgets.

Research has found that rural women are more likely to choose mastectomy over breast conserving surgery^{10 11}. Anecdotal stories from our members support these findings. Many rural women cite the extended time away from home for radiotherapy as a critical factor for choosing the more invasive form of surgery. The physical and psychological impacts of mastectomy versus breast conserving surgery are well documented. Many women in rural areas do not have the advantage of making a decision based on these factors alone, and may need to consider travel and time away from families and work ahead of clinical considerations.

The radiotherapy options for rural women are limited – either take six weeks away from family, work or farms... or have a full mastectomy. – Kerry

Further, Australian research has found that women treated in rural centres were less likely to receive radiotherapy following breast conserving surgery¹². The study researchers considered that the impact of extended travel times may contribute to this discrepancy.

The distance to radiotherapy made it hard. It would have been many hours to drive there and back in one day. So we decided to live in the city for the six weeks. But we were lucky to be

able to do this. I know of others who have had mastectomies (when lumpectomies were recommended) because the drive to and from radiotherapy would have been too much and they couldn't afford to move. – Woman with breast cancer

The side effects of external beam radiotherapy

Many women experience adverse side effects as a result of radiotherapy. Clinical research has documented these side effects, and the feedback from our membership suggests that the impact of these side effects can be considerable.

In April 2011, BCNA surveyed members of our Review & Survey Group about the issues faced by women who require radiotherapy. Two hundred and sixty-six members completed the survey. Most women told us they experienced skin changes that were like sunburn, including redness and burning. Thirty four per cent of women told us that their skin blistered, while just under a quarter experienced weeping. Nearly a third of women rated their discomfort level at eight or more out of ten.

I have terrible radiation burns that are very sore and weepy near my underarm on the bra line. This area has been radiation free for about a week, but continues to give me grief. – BCNA Online Network member

In addition to adverse skin reactions, many women experience fatigue. BCNA's 2011 Member Survey results, in addition to multiple reports from our membership and academic research, suggest that the fatigue can be extreme, debilitating, and will often develop at the end of the course of radiotherapy or even following its completion. Some women in the 2011 survey reported that the daily travel to the radiotherapy facility may have contributed to their fatigue.

The worst aspect of my treatment was fatigue. It was extremely debilitating and lasted many weeks after radiation finished- BCNA member

The benefits of intra-operative radiotherapy

BCNA and BCAC consider that affordable access to intra-operative radiotherapy as an option for eligible women with low risk breast cancers will go some way to improving outcomes for women who require adjuvant radiotherapy. A safe and effective single dose of radiation during the surgical phase of their treatment will mean women can complete their entire local treatment at the time of their operation, with lower toxicities and reduced time spent away from family and work commitments.

Feedback from BCNA members who participated in the Western Australia TARGIT trial was extremely positive with women reporting that they were pleased with the process and outcome.

I was happy not to have to leave home for six weeks of radiotherapy in Perth. The procedure was straightforward, with no side effects and only a little pain afterwards. – Carol, IORT trial participant

BCNA and BCAC believe that evidence relating to better outcomes for skin preservation should be considered during the decision-making process related to this application. We understand that the IORT technique involves less skin exposure than EBRT. Any beneficial outcomes for women, such as reduced pain, redness, blistering, and other skin changes frequently reported should be reviewed and considered alongside other clinical considerations.

Although neither BCNA nor BCAC are aware of any evidence related to the effect of IORT on fatigue, we consider that the reduced time spent travelling to, waiting in, and being treated in a radiotherapy clinic is very likely to have some impact on the fatigue levels of women with breast cancer following treatment. Fatigue is a commonly reported side effect of radiotherapy, and many of our members feel that the impact of this fatigue on their quality of life and recovery is frequently underestimated by medical professionals. We consider that any treatment option that reduces the fatigue of women with breast cancer will be a significant improvement.

Cost Benefits

The projected cost-saving benefits of IORT have been estimated to be in the region of several million pounds in the UK and substantially more in the USA, even without including time-saving and costs-saving benefits to the patient¹³ Availability of IORT for breast cancer patients may also assist to reduce waiting times for radiotherapy for people with other tumour types.

Summary

We note the findings of the international randomised TARGIT-A clinical trial showed that, for women with low risk breast cancers, IORT was safe, equivalent to whole breast radiotherapy in terms of local recurrence and breast cancer-specific mortality, and better than whole breast radiotherapy in terms of deaths from other causes, toxicity and tolerability.

BCNA supported the successful application to include IORT on the Medicare Benefits Schedule (MBS) in Australia while BCAC submitted to New Zealand's National Health Committee (NHC) that IORT should be introduced into New Zealand's public health system and is hopeful that this will occur following completion of the current NHC assessment.

In its consideration of targeted IORT, MSAC noted that the proposed MBS item criteria stemmed from the multi-national TARGIT-A trial upon which this submission is based. MSAC also noted that the TARGIT-A trial was a good quality, multicentre randomised control trial, the results of which showed women receiving targeted IORT experienced less toxicities than women in the two comparable treatment groups.

BCNA and BCAC are now calling upon the Faculty of Radiation Oncology to include IORT in its 2015 Horizon Scan Position Paper on Techniques and Technologies in Radiation Oncology for Australia and New Zealand so that women in our regions will have the same access as women attending more than 260 major breast cancer centres around the world.

We understand that the Faculty is concerned that the follow-up period in the TARGIT-A trial is too short and further follow-up should be awaited to assess these outcomes. The peak hazard of recurrence of breast cancer is in the first 2 to 3 years¹⁴. Whilst the risk of recurrence is never zero, as more time passes the risk goes down. We believe that women should be fully informed of all of the options available when having treatment discussions with their specialists and that this should include risk versus benefit conversations. A full discussion regarding the fact that the current follow-up period for IORT is short and that the recurrence rate and toxicity may be worse as the data matures, should be provided to women within the context that the highest risk of recurrence is likely to exist within the first two years from diagnosis.

BCNA and BCAC believe that many women with a good prognosis would choose IORT for the convenience, despite the short follow up period of the TARGIT-A trial. This belief is

supported by a recent study that examined patient preferences regarding IORT versus EBRT following breast conserving surgery that found that the majority of breast cancer patients will accept a small increment of local risk for a simpler delivery of radiation¹⁵.

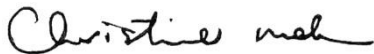
BCNA and BCAC believe that the level of evidence provided to date is sufficient to support provision of the option of targeted IORT with **appropriate informed consent**, for women who meet eligibility criteria, as determined by the TARGIT-A trial, and ask that RANZCR reconsider the conclusion of “insufficient evidence” drawn in their draft position statement.

The ease of access afforded by a single radiotherapy treatment will have significant advantages for groups of women whose outcomes are known to be poorer. This includes Indigenous Australian women, New Zealand breast cancer patients, and particularly Maori women. In addition, IORT has the potential to reduce the higher rates of mastectomy observed in rural populations. Cost saving benefits in a time of tightened health budgets should also not be underestimated.

We therefore ask that RANZCR support the timely introduction of this technique and technology.

If you require additional information or wish to discuss our submission further, please contact Kathy Wells at kwells@bcna.org.au or (03) 9805 2585 or Libby Burgess at celiam@breastcancer.org.nz.

Yours sincerely



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CEO BCNA



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