Dear Bijal:

I have read the material you very kindly sent me: it is extremely impressive and much work has clearly gone into it. And in a way, that is what worries me: it is so detailed, cites so many references, how can it be wrong? But I think that there are several erroneous assumptions, though I am of course not qualified to make any medical comments.

Both the Abstract (p 4) and the Plain English Summary (p 13) seem to me to be worryingly negative due to omissions. I feel they have cherry-picked data that suits their case, which is a cause of concern since many people will take these as reflections of the report conclusions. I assume this Assessment Report is only one among several submissions and that there will be other material to help make the NICE decision? But I would like to say:

1. The Abstract points out that '*A significant investment in INTRABEAM equipment and staff training (clinical and non-clinical) would be required to make this technology available across the NHS.'* But we know that the incidence of breast cancer is greatly increasing in our ageing population as the Report itself says. (45,000 of those presenting in one year will be over 45.*)
Much of the NHS radiotherapy equipment is old and in need of replacement. So both increased training and new equipment will be necessary anyway.

2. The Plain English Summary says, '*After BCS a three-week course of EBRT reduces the risk of breast cancer returning to the affected breast (local recurrence.)*' But it does **not** say that with EBRT there can be no repeat with this particular radiotherapy delivery because breast tissue will not tolerate

it. I understand that if breast cancer returns it may well do so in the same breast and even in the same quadrant. If Intrabeam was used, it could then be repeated because it is so precisely targeted, or EBRT is also an alternative. Both would allow a lumpectomy. But under current NHS practice, if EBRT has already been used, mastectomy may be the only recourse. But if there is recurrence after the use of EBRT, Intrabeam can be used - another argument for its adoption.
The Summary also fails to say that Intrabeam given during BCS is found to produce results similar to EBRT.

3. The Summary says '*the likelihood of dying from breast cancer was similar with both treatments…. but radiation therapy toxicity was less frequent than with EBRT.*'

On p.23 the Assessment Report says of EBRT '*short term adverse effects(eg skin soreness/redness, tiredness, nausea) and long term adverse effects (eg changes to breast size and texture/ feel, lung or heart problems)….*
This is surely a massive under-reporting of the facts as well as massive understatement. Damage to lungs or oesophagus (this not mentioned) can have terrible consequences, but the longterm effects of such damage are not referenced here. Yet we know that they can force drastic changes to lives. And it is now accepted that there is **no** level of radiation which does not adversely affect the heart.

There is here no reference to the fact that due to growing concerns about all the above, radiotherapy is now frequently given with the patient lying on her front in an attempt to protect organs.

Following whole-breast radiation, we know that non-breast cancer deaths or long term illness can be attributable to heart

damage and other cancers. With Intrabeam, the results of a major trial of 3,451 women in 33 centres worldwide (reported in The Lancet 11.11.13) showed that deaths from causes other than breast cancer were lower in the TARGIT trial group than in women who received conventional radiotherapy – only 1.3% as compared with 4.4%.

4. p.23: ' *EBRT is nearly always given when chemotherapy has been completed and after a gap of 2-3 weeks that minimizes overlapping and/or enhancing toxicities….*

I may have missed a reference to this – and if so, forgive me – but the gap in time between surgery and receiving EBRT may be months rather than weeks. And in that time, cancer cells can regroup, encouraged by wound fluid.

4. The Summary says ' *Intrabeam patients more frequently experienced fluid pockets that were drained more than three times.'* Of course fluid pockets have a potential for infection on an already compromised immune system. But draining is neither risky nor invasive, it can be carried out quickly, not in a theatre. There was no difference in wound infection rate or wound breakdown.

So less radiotherapy toxicity is surely a key consideration, particularly as it is a weighing of a single treatment against a regime of three or more weeks.

5. I found the research measurement on Quality of Life issues difficult to understand. From my own experience, Intrabeam is the perfect treatment. The speed, the ease, the knowledge that I did not have to wait weeks or even months for radiotherapy – I knew that cancer cells can regroup, and that wound fluid facilitates this – was incredibly reassuring at a time when I was physically and emotionally vulnerable.

6. The report itself goes into detail about the ageing UK population and the resulting increase in breast cancer among older women. The Summary concludes *'The longer term effects of INTRABEAM are not known and further research on this is needed.'* True. But women in their late forties and fifties must be among the busiest of people, the majority of them juggling young families with careers and jobs. A long period of inactivity for them is desperately difficult – and expensive. They need fast and effective treatment now, not at some undefined future time.

To tell an older woman – I was 69 –to wait while further research is carried out, is unnecessarily cruel. She may not live to benefit. The fact that the treatment has been followed in one of the biggest international breast cancer trials ever run, over twelve years, (above) was proof enough of its efficacy for me and, I am convinced , for others. We have no time to wait.

I believe that to deny appropriately selected women INTRABEAM (TARGIT) on the NHS any longer would be a real mistake. For a patient, to be spared the unpleasantness, dangers and possibly hazardous long-lasting effects of EBRT, to know that for five years at least she will almost certainly be safe, is reason enough to choose it. And – again as I understand it – once ten years has elapsed since surgery, there is no difference in local recurrence between treatment with EBRT and that with Intrabeam.

It should go without saying that any woman must not only meet the clinical criteria but be fully informed of the risks and benefits of both treatments.

Yours sincerely,
Marcelle Clark
* Cancer Research UK incidence data