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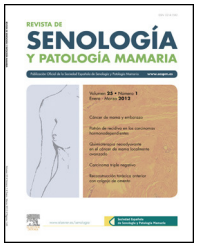

EDITORIAL

Two sides of the spectrum: Improving local control in young patients and decreasing treatment burden in low risk patients

Dos aspectos del espectro: mejorar el control en pacientes jóvenes y disminuir el tratamiento en pacientes de bajo riesgo

Breast cancer is not a unique disease but includes a wide spectrum of diseases with a different clinical behaviour based on patient and tumour related factors. Treatment should be individualised to this in order to obtain the best results for local control, distant metastases free survival and overall survival. While research to further intensify treatment in patients with a poor prognosis like young women with locally advanced triple negative breast cancer should continue, we have to keep in mind not to over-treat patients with a favourable risk profile to optimise not only survival but also quality of life for the entire patient population.

In this first issue of 2014, 2 articles focussing each on 1 end of the spectrum of breast cancer are published. The first one focuses on using a single fraction of HDR-brachytherapy as a boost to the primary tumour bed in the framework of breast conserving therapy (BCT) in patients up to 45 years of age.[1] The EORTC boost–no-boost trial clearly demonstrated that a boost of radiation to the primary tumour bed in the framework of BCT improves local control by reducing the local recurrence (LR) risk with 41%.[2] The most important risk factors were age and tumour grade while later on it was also confirmed that the use of adjuvant systemic therapy reduces the LR risk.[3,4] The addition of a boost reduced the LR rate with the same relative percentage independent of the risk factors but as the absolute LR rate varied widely depending on patient and tumour related risk factors, the absolute reduction of LR ranged from >10% at 10 years in patients up to 40 years of age to <4% at 10 years for patients older than 50 years. No influence on overall survival could be demonstrated. Unfortunately, the risk for development of moderate to severe fibrosis depends strongly on the total dose given.[5] It also had a clear impact on overall cosmetic outcome with 86% good to excellent results without a boost and 71% with a boost.[6] Therefore, the value of a boost to the primary tumour bed is most expressed in patients at a higher risk of LR, including younger patients. The article in this issue focuses on a specific technique to deliver a boost in patients up to the age of 45 years. The results in terms of local control are excellent and confirm the impressive decrease in the local recurrence rate after BCT as shown in younger patients earlier.[7] Therefore, age as such should no longer be considered as a contraindication for BCT. The series of Guinot et al. is unfortunately too small to clearly demonstrate an age effect on local control below the age of 45 years to further exclude an elevated risk in very young patients.

In the EORTC trial, the technique that was used to deliver a boost had no significant impact on the results.[8] Each of them has advantages and disadvantages. When delivering the boost after completion of whole breast irradiation (WBI), full knowledge of the pathology report can be used to individualise the margin surrounding the primary tumour bed and the volume reduction of the surgical bed over time will reducing the boost target volume.[9,10] Brachytherapy is an invasive procedure but Guinot et al. reduced the impact of this by performing it under local anaesthesia and sedation on an outpatient basis. Moreover, as demonstrated earlier, with modern techniques a very conformal dose to a small volume can be delivered with supplementary advantages that the radiation does not have to pass through healthy tissue like the skin and that no margin from clinical target volume to planning target volume is required.[8] This for sure explains the excellent cosmetic outcome as reported by the authors.[1]

And then back to the other side of the spectrum. Rodríguez et al. revised especially the technical aspects of the still growing variety of approaches developed for delivering accelerated partial breast irradiation (APBI) in patients at low risk for developing a local recurrence.[11] APBI emerged at the end of the nineties especially because of the observed inconvenience of the long treatment duration of standard whole breast irradiation (WBI) with or without boost, leading to a high mastectomy rate and a clear underutilisation of RT after surgery along.[12] The aim was thereby to reduce the overall treatment time from 5–7 weeks to 1 week or even shorter so that more patients could benefit from BCT. To enable this, the treated volume needed to be reduced,

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leading to the concept of partial breast irradiation. While originally interstitial brachytherapy and external beam RT were used, a wide number of techniques and tools have been introduced over the last 15 years. However, due to the specific technical aspects of each of them, marked differences in (radiobiologically equivalent) dose and treated volume can be observed. Others also warned against the possible underdose to important parts of the highest risk target volume.[13] Therefore, long term results of preferably prospective studies are required to reliably esteem the true value of each of the APBI techniques separately, as they for sure cannot extrapolated from one technique to another.

Whereas several quite promising results are presented and published, we should recognise that unfavourable results in terms of cosmetic outcome were published as well and that optimally long term outcome (at least 8–10 years) should be awaited for as most of the patients eligible for APBI also receive adjuvant hormonal therapy which will delay the occurrence of local recurrences.[14] Therefore, many of the presented APBI results could rather be compared to the outcome after lumpectomy and hormonal treatment alone.[15] Moreover, several of the past and ongoing trials used assumptions to calculate non-inferiority statistics based on the results obtained with BCT dating from the eighties, not taking into account the decrease in the local recurrence rates with a contemporary treatment approach.[7] Therefore, the old upper limit of 1–2% local recurrences per year should rather be replaced by a maximum of 0.5% to truly esteem the results of APBI and not to jeopardise the improvement in outcome obtained in more recent years by optimising as well local as regional and systemic treatments.

The great premise of APBI was to reduce treatment duration from 5–7 to less than 1 week. However, hypofractionated WBI reducing the overall treatment time to around 3 weeks is being introduced widely all over the world after the publication of long term results of prospective trials, and is also accepted in some of the ongoing APBI trials including IRMA.[16,17] Further reduction of WBI to 1 week in 5 fractions, using modern RT-techniques enabling the delivery of a very homogeneous dose, is currently under investigation. If this proves to be a valid approach, the most important incentive supporting the use of APBI might disappear.

Whereas I do agree with the authors that APBI will highly probably become a validated standard approach for a selected subgroup of patients, I want to warn against an overenthusiastic interpretation of the published guidelines and (mainly short term) results by offering APBI to a wide range of breast cancer patients. I would rather encourage to invest in new prospective trials comparing the true merits in terms of local control and quality of life of local treatments (WBI versus APBI versus nothing) and adjuvant systemic treatments (hormonal treatment versus nothing) for low risk breast cancer patients. It might very well be that 3 weeks of WBI without systemic treatment comes out as the winner in a quite large subgroup of low risk patients.

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