HER-2 subtype and age affect local control in breast cancer. OC-0203
also has a significant effect on late breast toxicities.

Purpose/Objective: Radiation therapy (RT) significantly ameliorates local control in breast cancer (BC) patients treated with breast conserving surgery and in high relapse risk radically resected patients. Some debate exist about the value of RT in elderly patients. In this retrospective analysis on a single institution series of BC patients we evaluate local control as regard to age and different prognostic factors.

Materials and Methods: Patients undergoing postoperative RT for localized breast cancer treated at our institution between January 1999 and December 2008 were the object of the study. RT consisted of 50 Gy in 5 weeks on the chest wall, in the case of mastectomy, and on residual breast in the case of quadrantectomy or lumpectomy, and eventually on the axillary and supraclavear nodes. A boost of 10 Gy was administered to the tumor bed of all the conserving surgery treated patients. The clinical data were analyzed with univariate and multivariate analysis considering age (<40, 40-64, ≥65), nodal status (N+ vs N-), tumor classification (T1 vs T1), grading (G1-2 vs G3), oestrogen and progesterone receptors (ER and PgR), and erb-B2 status. A further classification of patients according to a surrogate approximate genetic signature and recognizing the four subtypes of BC, namely luminal A (ER+ and/or PgR+), and erb-B2-) luminal B (ER+ and/or PgR+ , and erb-B2+), erb-B2 subtype, and basal(ER−, PgR− and erb-B2−) was adopted. Freedom from loco-regional relapse (FFLR) was defined as the time from diagnosis to the loco-regional relapse (LR). The 8-year LR rate was estimated by the Kaplan-Meier method.

Results: Seven hundred thirty-three patients with a median age of 53 years (range 27-84) and with a minimum follow up of 12 months entered the study. Chemotherapy, hormonal therapy or both, were administered in 57, 374, and 249 patients, respectively. The median follow up was 84 months (range 12 – 126), with an overall survival of 96%. The 8-year actuarial rate of LR was 3%. Univariate analysis showed a significant relation of LR with age (LR=6.1% for age<40 years, LR=1.6% for 40≤age<65, LR=6.5% for age≥65), grading (LR=1.7% for G1, LR=4.1% for G2, LR=5.4% for G3), ER status (LR=2.3% for ER-, LR=5.4% for ER+), HER2 subtype (LR=2.3% for no-HER2, LR=8.5% for HER2). From the multivariate analysis, the hazard risk 3.9 for age≥65 years and 3.23 for age 40-40 years compared with 40≤age<65 and HER2 subtype (hazard risk3.8) were the only significant factors for LR risk prediction (Fig.1).

Figure 1

Conclusions: Age less than 40 and equal to or more than 65 years and HER2 subtype are associated with a greater risk of local relapse. These results do not support a different RT management of elderly patients.

SYMPOSIUM: RESHAPING THE STRUCTURE OF RADIOTHERAPY CENTRES FOR 2020

SP-0204
Planning of radiotherapy capacity: Lessons from The Netherlands
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Background: Although radiotherapy is a very cost-effective treatment modality, it requires major investments for building and equipment. Adequate planning of radiotherapy infrastructure and personnel may prevent waiting lists and over-capacity with vacancies. In the Netherlands, until recently, radiotherapy capacity was regulated by the government. Until 2000 this was done by a limitation of the number of linear accelerators and since then by a limitation of the number of centers. Models have been used to estimate the expected number of cancer patients, patients requiring radiotherapy and the distribution over different types of treatment (simple, standard, intensive, or special). This was used to determine the required numbers of machines and staffing. The actual situation in the Netherlands is evaluated annually by a survey of all Dutch centers.

Materials and methods: For the period from 1998 to 2010, the predictions from the Dutch Society of Radiotherapy and Oncology were compared with the actual measures from annual surveys of the 21 Dutch centers. In addition, developments of productivity and departments size are evaluated.

Results: An annual increase in the number of patients and radiotherapy treatments of 3.5-4.0 % was observed. The number of machines and staffing increased accordingly. After a relative increase in the percentage of 3D conformal treatments in the late 1990s and early 2000s, a shift from 3D-conformal techniques to intensity modulated, image-guided and stereotactic techniques was seen in the later years. In 2010, 39% of the treatment series was delivered using IMRT, IGRT, SBRT or radiosurgery techniques, 21% using 3D-conformal techniques an 40% using standard techniques. In 1998, their were 274 treatment series per radiation oncologist, 625 per physicist and 532 per linear accelerator, compared to 249 series per radiation oncologist, 540 per physicist and 451 per accelerator in 2010. The number of radiotherapy departments did not increase over the study period. The average size of the centers was 5.7 accelerators, 10.4 fte radiation oncologists, 4.8 fte clinical physicists and 45.8 fte technologists, compared to 3.2 accelerators and 6.2 fte, 2.7 fte and 30.4 fte, respectively in 1998.

Discussion: Prognoses of the number and types of radiotherapy treatments allow for an accurate prediction and planning of the required staffing and infrastructure to avoid waiting lists and over-capacity. The expansion of the existing departments instead of the addition of new centers, allows for a more rapid implementation of new techniques and will allow sufficient sub-specialization of the staff. In recent years, the expansion of departments is often realized by establishing ‘satellite centers’, which are an integral part of the main center. Treatment planning is performed at the main site and the staff rotates over the satellite(s) and the main center.

SP-0205
Needs versus provision: how does the UK tackle this problem.
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Historically, England has faced an under-provision of radiotherapy, due in part to the decentralised nature of equipment procurement and workforce management. The ESTRO QUARTS, a report commissioned by the National Radiotherapy Advisory Group, suggested that by 2016, activity levels of 54,000 fractions per million/year would be required. The report recommended a long term strategy for the development and expansion of a multi-professional workforce for radiotherapy delivery, the expansion and modernisation of radiotherapy delivery services, the central collection of radiotherapy treatment statistics, and improvement in treatment quality starting with IMRT and moving over a decade to 4-D adaptive radiotherapy. A National Radiotherapy
Implementation Group (NRIG) was established to implement these recommendations. The NRAG model of radiotherapy demand was seen as overambitious and unrealistic for the Malthus project was commissioned to review and update the work. Malthus is an academic initiative to provide adscription event tool for simulation of radiotherapy demand in the U.K. at a local level. Launched in October 2011, the tool provides radiotherapy service managers and healthcare commissioners with a customizable model that can quantify radiotherapy demand at the level of the primary care trust (mean population = 330,000) or cancer network (mean population = 2,300,000). Clinical decision making is encoded into disease specific decision trees, established by a review of current evidence-based practice for radiotherapy. The tool uses curated data feeds from the national cancer intelligence network to provide accurate local population demographic and cancer incidence data. Models for population growth and change in cancer incidence are used to forecast radiotherapy demand through to 2030. The estimate of radiotherapy demand for the U.K. as a whole for 2016 is 55,000 fractions per month, closely similar to that of NRAG. To encourage expansion of radiotherapy there is now a nationally-agreed tariff and the service will be commissioned nationally. The Radiotherapy Dataset (RTDS) collates information on treatment activity via electronic feeds from all radiotherapy centres in England. Monthly data uploads have been mandatory since April 2009, and data feeds from RTDS are available with a 12 month latency from the Cancer Commissioning Toolkit. These data can be compared to the Malthus model in order to understand radiotherapy provision for the local population. As local data on stage and performance status become available it will be possible to assess the influence of these factors on the uptake of radiotherapy and whether or not they have a significant influence in addition to under-investment. IMRT delivery has increased from 2% of patients in 2008 to 11% of all patients in 2012. It is expected that IMRT will be offered to the 33% of radically treated patients who would benefit by the end of 2013. A national programme to support IMRT training, implementation, and quality assurance has been established to overcome the barriers including staff shortages, lack of agreed funding for IMRT, and low levels of training in IMRT implementation. The expansion of IGRT will then pave the way to the development of 4D adaptive radiotherapy as envisaged in the NRAG report of 2007.

Because of inevitable uncertainties in RT, margins assure that the prescribed dose is actually absorbed in the target. A major breakthrough in thinking about margins occurred with the appearance of ICRU50, standardizing terminology. Around the same time, random errors, that affect each treatment fraction differently, and systematic errors that affect all fractions in the same way were differentiated. A second breakthrough occurred in the nineties when it was realized that you have to make a trade-off between the risk of under-dosing the target that reduces with bigger margins, versus the risk of overdosing normal tissues that increases with bigger margins. This trade-off is then expressed as the probability of a certain underdose of the target. Using then plausible uncertainty data for the prostate, it appeared that a 90% probability of delivering 95% of the prescribed dose in the target required a then routine 1 cm margin. I.e., these numbers were apparently clinically acceptable and they formed the basis for the (simplified) NKI margin recipe: $M = 2.5 \text{SIGMA} + 0.7 \text{sigma}$. Many authors have challenged and refined this publication but it is still being widely used. The equations works well for a wide range of situations and are safe if you adjust the SIGMA and sigma for the number of fractions given. Then what are the problems with margins? First, they do not take the beam and patient geometry into account. E.g., a high dose is assumed even where the margin overlap an organ at risk, while the probability of the target being in that location during treatment may be very small. Ad-hoc adjustments are therefore often made, but this makes it very difficult to assure robustness or even estimate the level of robustness of the modified plan. Finally, with painted dose distributions, no simple margins recipes exist.

How are we going to deal with these problems? Well there is only one good solution, margins have to go! By incorporating the knowledge about residual uncertainty distributions directly into IMRT planning, regular dose distributions are sculpted that take the actual shape of the dose distribution and the location of organs at risk into account when generating a margin. A number of publications have investigated this approach, demonstrating the possibility to develop plans that are just as robust as their margin-based counterparts, but with much lower exposure of the organs at risk. The resulting plans look very sensible, e.g., similar to integrated boost approaches with reduced margins towards organs at risk but with guaranteed robustness. And why is not everybody using this approach if it is cleaner better? This is because so far planning system vendors have refused to invest in this approach. Hopefully this situation will change soon.

The European viewpoint: ESTRO-HERO experience

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Based on detailed evidence-based modeling, radiotherapy has been identified as a necessary component of the oncological treatment in on average 52% of all newly diagnosed cancer patients. Such estimates are important to help forecast radiotherapy resource and personnel needs. But when applied to different countries, such as in the highly variable European context, one should be aware that they are sensitive to the demographic and socio-economic factors in these countries and to changes in incidence, population mix and stage distribution over time.

In the early years 2000, the ESTRO-QUARTS-project used a combination of epidemiology, evidence-based radiotherapy indications and resource use to evaluate the differences in needs amongst 23 European countries. Along with this modelling exercise, it also suggested benchmarks for a robust and personalized demand data and cost-accounting models for radiotherapy. Finally, these data will also form the basis for cost-effectiveness analyses to evaluate the value for money of radiotherapy innovations and of radiotherapy compared to other oncologic treatments.

SYMPOSIUM: RETHINKING MARGINS IN THE DAILY-IGRT AND/OR ART CONTEXT

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