

## SP-0617

## IMRT for lung cancer: current status and future developments

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IMRT is a technique that adds fluence modulation to beam shaping, which improves radiotherapy dose conformity around the tumour and spares surrounding normal structures. Treatment with IMRT is becoming more widely available for the treatment of lung cancer, despite the paucity of high level evidence supporting the routine use of this more resource intense and complex technique [Chan. *J Thor Oncol* 2014]. It allows the treatment of patients with large volume disease, close to critical organs at risk with curative doses.

Very few prospective trials have reported on the use of IMRT. RTOG 0617 was a 2 x 2 factorial design study, in which patients with stage III NSCLC were randomized to receive high dose (74 Gy in 37 fractions) or standard dose (60 Gy in 30 fractions) RT concurrently with weekly paclitaxel/carboplatin with or without cetuximab [Bradley. *Lancet Oncol* 2015]. The radiotherapy technique (3D conformal RT vs IMRT) was a stratification factor. Disappointingly, there was a significant increase in the risk of death in the high-dose arms (median survival, 19.5 months vs 28.7 months;  $p=0.0007$ ), and a 37% increase in the risk of local failure in the high-dose arms (hazard ratio, 1.37;  $p=0.0319$ ). It should be noted that just under half of the patients in this study were treated with IMRT (46.5%). Although patients were stratified by treatment delivery technique and the proportions of patients treated with IMRT were balanced between treatment groups (46.1% in 60 Gy arms and 47.1% in 74 Gy arms), the delivery of 74 Gy was probably challenging, particularly in patients treated without IMRT, given the gross tumour volume (GTV) (mean 124.7 in 60 Gy arms and 128.5 cc in 74 Gy arms).

A subsequent analysis on patient reported outcome demonstrated a significantly worse quality of life on the 74 Gy arms at 3 months after treatment [Mosvas *JAMA* 1015]. Interestingly, despite minimal differences in clinician-reported side-effects between treatment arms, the decline in quality of life was significantly reduced with the use of IMRT compared to 3DCRT suggesting that the use of improved radiotherapy treatment techniques may be beneficial. Furthermore, baseline QOL was an independent prognostic factor for survival. A further analysis of RTOG0617 compared the outcome of patients treated with 3D-conformal and intensity modulated radiotherapy [Chun. *ASTRO* 2015]. Survival was the same in both groups in spite of the larger proportion of patients with stage IIIb vs IIIa and larger Planning Target Volume in the IMRT cohort. Moreover the use of IMRT reduced severe pneumonitis, dose delivered to the heart and more patients received chemotherapy in the IMRT cohort.

Population-based studies have not shown any significant difference in overall survival, toxicity or time spent hospitalized following treatment between 3DCRT and IMRT [Harris. *Int J Radiat Oncol Biol Phys* 2014; Chen. *J Thorac Oncol* 2014]. The need remains to develop clinical trials that will demonstrate the benefit of IMRT in terms of toxicity, local control, survival or quality of life.

A number of clinical trials are currently recruiting patients. Some are evaluating personalized dose escalation based on dose delivered to organs at risk (NCT01836692, NCT01166204) and others an increase dose to selected parts within the tumour, defined by functional imaging (Dose Painting) (NCT01024829, NCT01507428).

## SP-0618

## Are there early and late benefits of breast IMRT for improving dose distribution homogeneity?

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In countries with active mammography screening programs, the majority of breast cancers are diagnosed at an early

stage. Those patients are treated with breast conserving surgery followed by adjuvant radiotherapy, which is equivalent to mastectomy in term of survival. The objective of the radio-surgical association is hence primarily cosmetic. Since those patients have excellent outcomes, it is logical to minimise any detrimental effects of the treatment, in term of acute and delayed side effects.

Intensity Modulated Radiation Therapy (IMRT) is a radiation technique where the photon beam intensity is modulated across multiple irradiation fields to achieve a pre-determined goal for the dose distribution, using try and error methods. The goal can be to improve the conformality of the dose distribution or, as it is often the case for the breast, its homogeneity.

There are many cohort studies and randomised clinical trials reporting on the clinical benefit for BIMRT used to improve the dose distribution homogeneity in the breast. A multicentre randomised controlled trial from Canada has demonstrated a large and significant reduction of acute skin toxicity, notably the moist desquamation occurring on the infra-mammary fold. This benefit was not present for large breasted patients. Moist desquamation was significantly associated with a severe pain and a reduction of Health Related Quality of Life (HRQoL). There are several studies reporting significant associations between the occurrence of moist desquamation and delayed side effects like telangiectasia and induration. Several randomised trials have also evaluated the impact of BIMRT on long-term side effect, and two studies from the UK using hypofractionated regimen showed a small but significant improvement of the cosmetic outcome at 5 years. It is important to note that no cosmetic improvement was found at 8 years in the Canadian study using conventional fractionation of 50 Gy in 25 treatments. In the Cambridge and Canadian studies there was no impact of the radiation technique on the long-term HRQoL. In the Canadian study there was a highly significant correlation between the initial pain experience at time of radiotherapy and the occurrence of chronic pain and a reduction in HRQoL at 8 years. Also the occurrence of moist desquamation at the time of radiation treatment was significantly correlated with the occurrence of telangiectasia, fibrosis and a poorer cosmetic outcome on self-evaluation questionnaire. Those studies suggest a complex interplay between the breast volume, the dose-fractionation schedule and the radiation technique. More recently, a study from Ghent demonstrated that for large breasted patients hypofractionated prone BIMRT significantly reduces moist desquamation compared to hypofractionated supine BIMRT.

In summary, there are solid evidences to suggest that BIMRT reduces the occurrence of acute skin toxicity, including moist desquamation and pain. For large breasted women, the use of a prone technique BIMRT appears to significantly reduce moist desquamation. In regards to long-term side effect it seems that BIMRT could improve the cosmetic outcome when using hypofractionation, but its role is less clear when using a standard dose-fractionation regimen. A painful experience of moist desquamation during the initial radiation treatment is significantly associated with chronic pain and poorer HRQoL. Since BIMRT is a technique relatively simple to implement at no cost, outside the USA, it should be used as standard for adjuvant breast radiotherapy.

## Symposium with Proffered Papers: Plan of the day (PotD): current status

## SP-0619

## PotD external beam: overview of current practice

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Most image guidance strategies today aim at minimizing random and/or systematic geometrical uncertainties by offline or online correction protocols based on either