Factsheet for the Press (Physics)

ADAPTATION OF RADIOTHERAPY TO A SHRINKING MACROSCOPIC TUMOR IN ADVANCED STAGE NSCLC (NON-SMALL-CELL LUNG CARCINOMA) DOES NOT UNDERDOSE THE MICROSCOPIC DISEASE AND HAS THE POTENTIAL TO INCREASE TUMOR CONTROL PROBABILITY

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Context: The combination of radiotherapy and chemotherapy is the current standard treatment for locally advanced non-small cell lung cancer (NSCLC). Before the start of radiotherapy, a computed-tomography scan (CT) is acquired for individualization of radiotherapy to the patient-specific tumour size, shape and position. However, a continuous shrinkage of the tumour during radiochemotherapy is well known, which opens the question whether radiotherapy could / should be adapted to this shrinking tumour during treatment: this could spare health tissue and in consequence reduce toxicity. This reduction of toxicity could be used to intensify the treatment aiming at improving the dismal prognosis of locally advanced NSCLC.

Purpose: Weekly CT images were acquired during radiochemotherapy of 13 patients with locally advanced NSCLC, where continuous tumour shrinkage of 50% was observed. In a retrospective planning study, we investigated the effect of adapting radiotherapy repeatedly to this tumour shrinkage; this was compared with the current standard of delivering the total radiotherapy based on the tumour size and shape seen BEFORE start of treatment. It was modelled, whether such an adaptive, patient-individualized treatment results in lung sparing and reduction of toxicity, which then allows intensification of radiotherapy. Special focus was simulation of safety of such an adaptive radiotherapy protocol: radiotherapy needs to treat not only the visible macroscopic tumour but also the invisible microscopic disease around the tumour, which may or may not shrink synchronously with the macroscopic tumour.

Findings:

1) Compared to current clinical practice, early and repeated adaptation of radiotherapy to the shrinking tumour spares healthy lung tissue significantly, which allows intensification of radiotherapy by 10% on average - with large differences between individual patients.

2) This adaptation of radiotherapy to the shrinking visible macroscopic tumour did not compromise treatment of the invisible microscopic tumour, irrespective whether a synchronous shrinkage of microscopic and macroscopic tumour or a stationary microscopic disease despite macroscopic tumour shrinkage was simulated.

3) Standard radiotherapy was modelled to achieve local tumour control in only 20% of the patients. Adaptive radiotherapy should increase tumour control by 50% on average to absolute control rates between 16% and 60%.

Impact: It is well known that intensification of radiotherapy will improve local tumour control which will then improve overall survival of patients with locally advanced NSCLC. Consequently, this adaptive radiotherapy technique has the potential to improve survival of the patients.

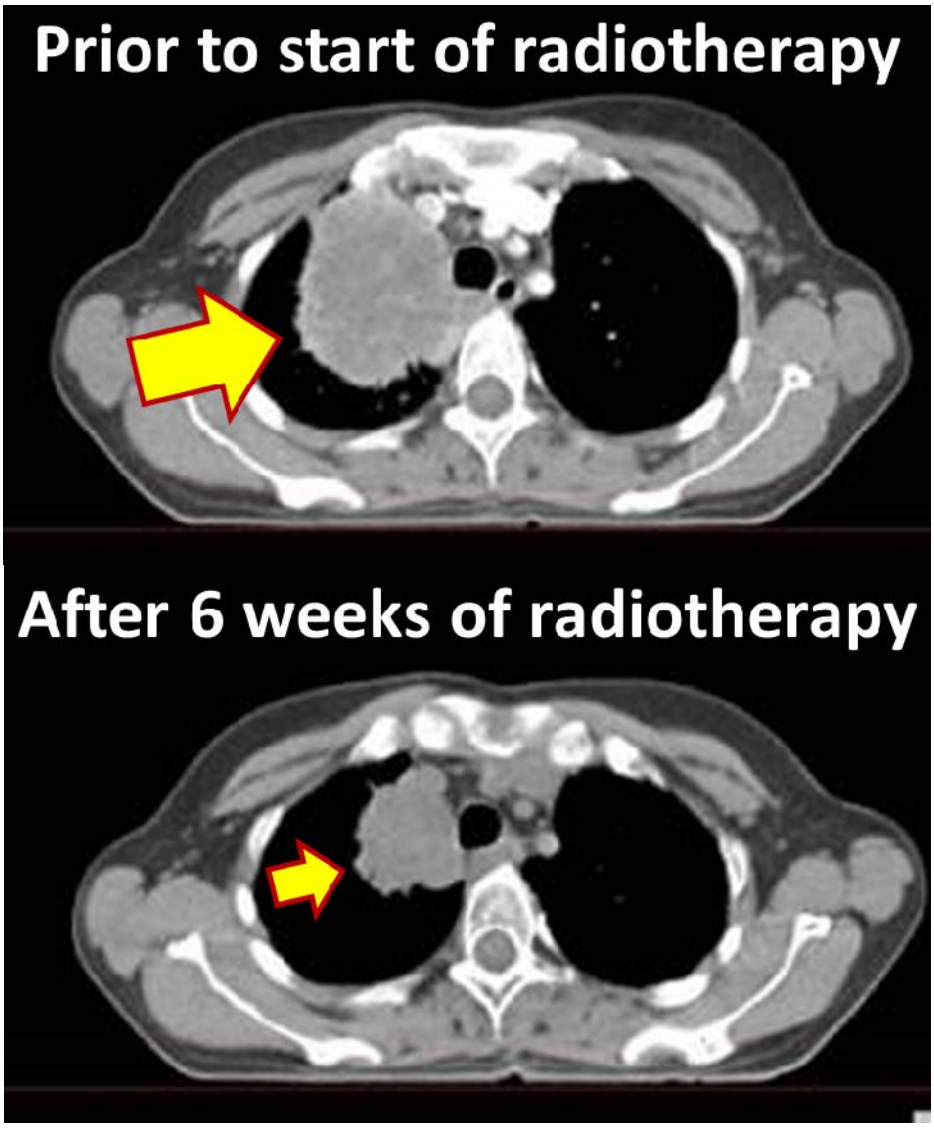
However, the hypothesis generated in this trial needs to be confirmed on a larger patient collective and with clinical outcome data.

The repeated imaging and adaptation of radiotherapy is associated with substantial work-load any may exceed capacities of certain radiotherapy department. Consequently, techniques and methods need to be developed for automation of the adaptive planning work-flow.

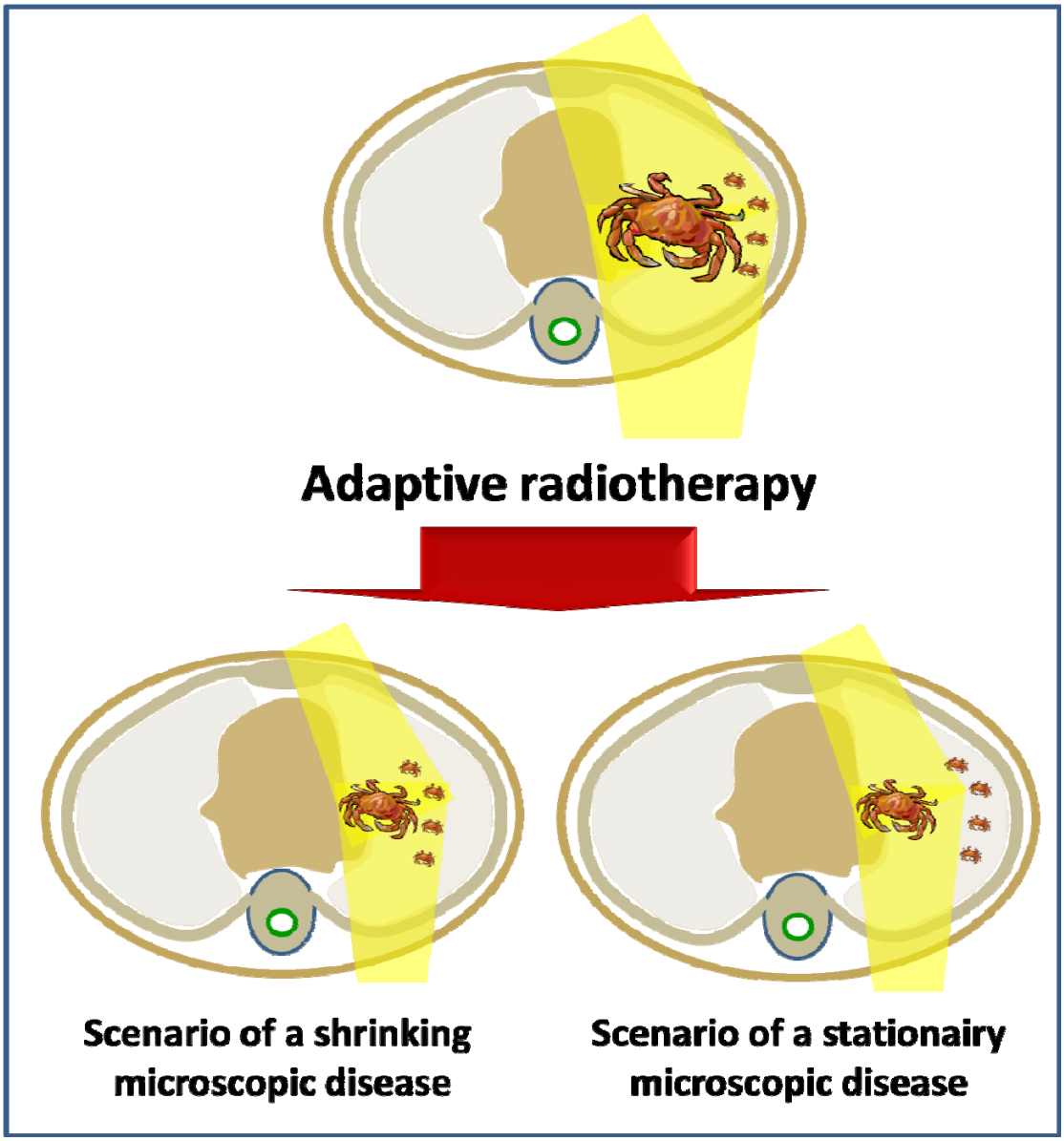
Indicative of a bigger trend in oncology? The described process of adaptive radiotherapy follows the current goal in Medicine in general and Oncology in particular of treatment individualization best and closest as possible to the patient-specific tumour characteristics and behaviour. Aim is maximization of survival and quality-of-life for each individual patient while minimizing the risk of severe toxicity.

"The message to take back home is that when adapting to shrinking macroscopic tumour we have to increase dose to the treated volume so that the dose received by the initial GTV+margin won't be compromised"

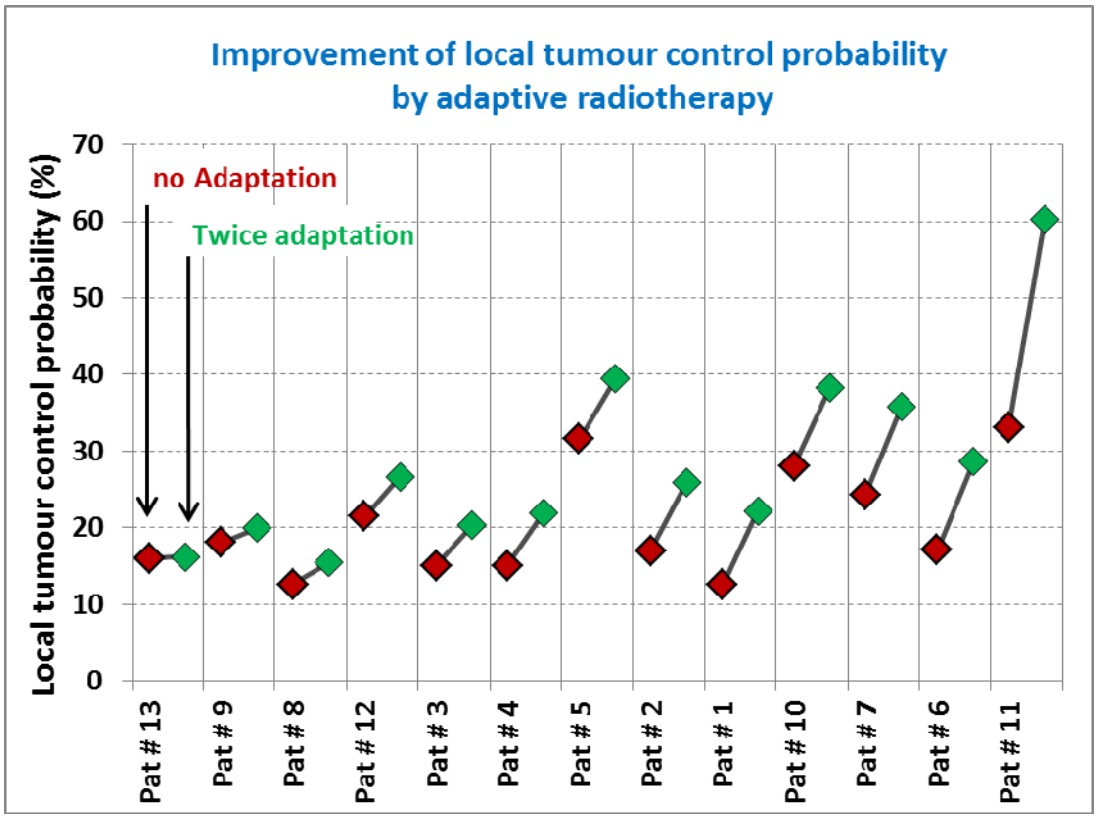
Dr Nuria Jornet, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain



Shrinkigae of a lung tumour during a 6 weeks treatment of combined radiochemotherapy.



Schematic illustration of adapting radiotherapy to a shrinking tumour during the treatment course. Two scenarios were simulated: synchronous shrinkage of microscopic and macroscopic tumour and a stationary microscopic disease despite macroscopic tumour shrinkage.



Patient individual gain (local tumor control) from adapting radiotherapy twice during the treatment course compared to delivering the total irradiation dose based on the tumour size and shape as seen before the start of treatment.