ESTRO

NEWSLETTER NOVEMBER-DECEMBER

ESTRO | EUROPEAN SOCIETY FOR RADIOTHERAPY & ONCOLOGY

SOCIETY LIFE

Technical Innovations and Patient Support in Radiation Oncology - tipsRO: **meet the editors**

PHYSICS

Bridging the gap between radiation oncology and surgery

CONFERENCES

International Conference on innovative approaches in Head & Neck Oncology (ICHNO): interview with the ESTRO chair

N° 109 | BIMONTHLY | NOVEMBER - DECEMBER 2016

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View of Vienna - Austria, where ESTRO 36 will take place, 5-9 May 2017.

ESTRO | EUROPEAN SOCIETY FOR RADIOTHERAPY & ONCOLOGY

RESEARCH PROJECTS

The ARTFORCE project; a tour de force well under way

The ARTFORCE project (Adaptive and innovative Radiation Treatment FOR improving Cancer patients' treatment outcomE) is funded by the EU 7th Framework Programme.

THE ARTFORCE CONSORTIUM

nine European academic hospitals

two European SMEs

ESTRO

expertise in basic / translational / clinical research

HARRY BARTELINK

This project is aimed at improving the therapeutic ratio for lung, and head and neck cancer by redistributing the dose of radiation, ensuring 3D quality control, and *in vivo* predicting sensitivity for radiation and cisplatin. This project consists of two main clinical trials in head and neck cancer, and lung cancer. Both trials are supported by a number of work packages for adaptive image guided radiotherapy, with functional imaging, as well as translational research for predicting treatment outcome. Here is a selection of the progress reports presented during the partners' meeting at ESTRO 35 in May 2016 in Turin, Italy, www.cancerartforce.eu ▼

CLINICAL TRIALS

PET-Boost lung cancer trial

José Belderbos / Dirk de Ruysscher

The randomised phase II trial: dose-escalation by boosting radiation dose with a homogenous dose to the primary tumour, or by boosting within the primary tumour to the 50% maximum standardised uptake value area on the pre-treatment FDG-PET-CT scan in stage IB, II and III non-small cell lung cancer (NSCLC).

The endpoint is local progression free survival. Extensive imaging of the tumour response is performed before and after treatment.
An independent data monitoring committee (IDMC) meeting was scheduled after a scheduled toxicity analysis. The IDMC recommended continuation of the study, but advised an extra check for contouring, exclusion of tumours with growth in large vessels on spiral CT scan and / or more than 50% encasement of a large vessel, as well as reduction of the volume of the D-max on the mediastinal envelope (from 0.1 volume-% to 1 cc). Based on these recommendations an amendment was installed and after approval of the MEC the trial is now open again for inclusion.

ClinicalTrials.gov Identifier: NCT01024829

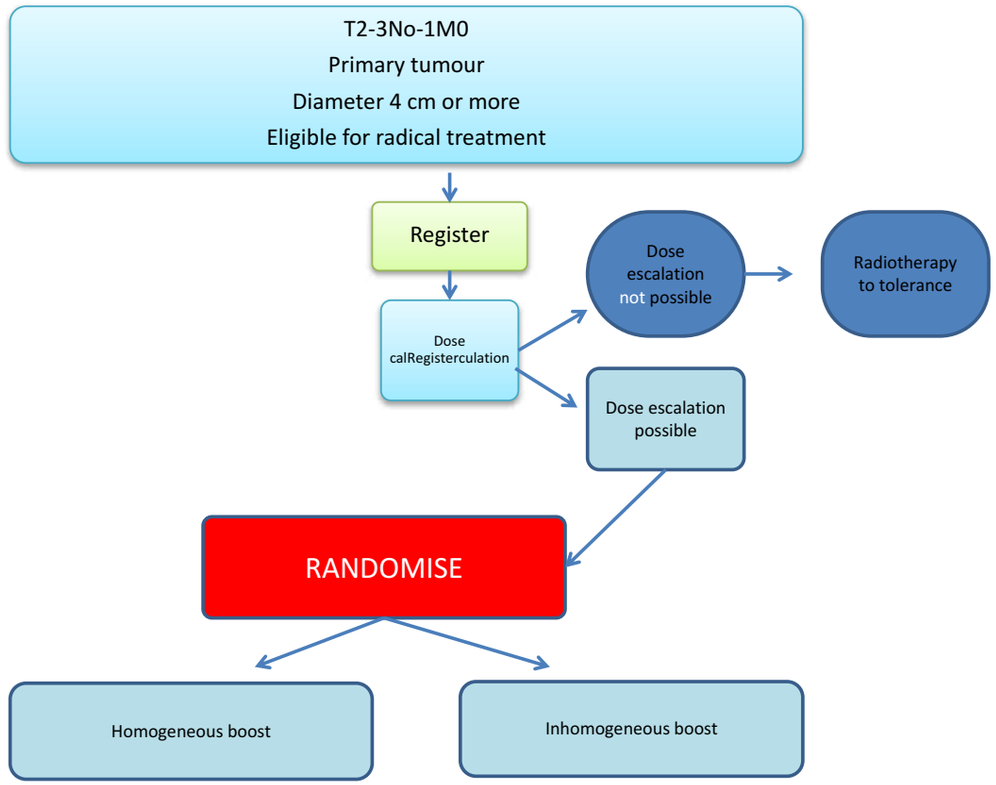
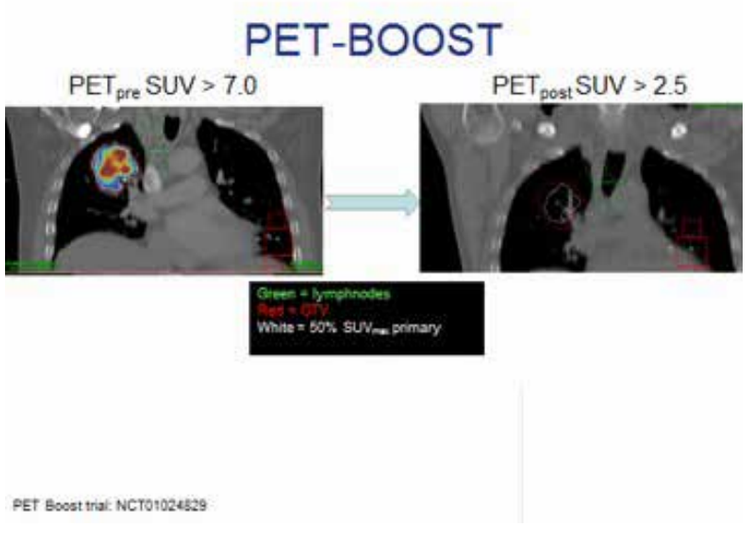
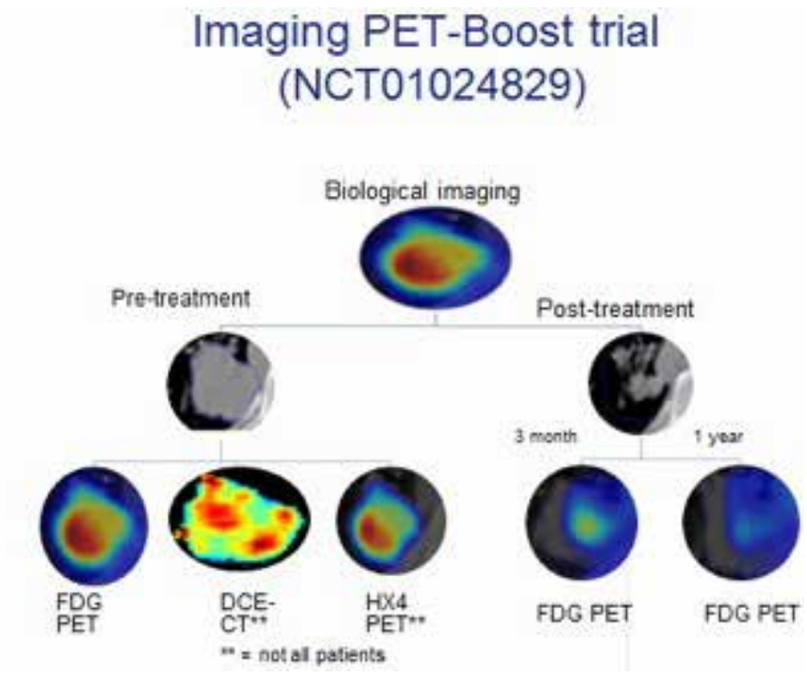


Figure 1: trial scheme





(Matthew la Fontaine)

Figure 2A and 2B: PET-CT imaging before and after treatment

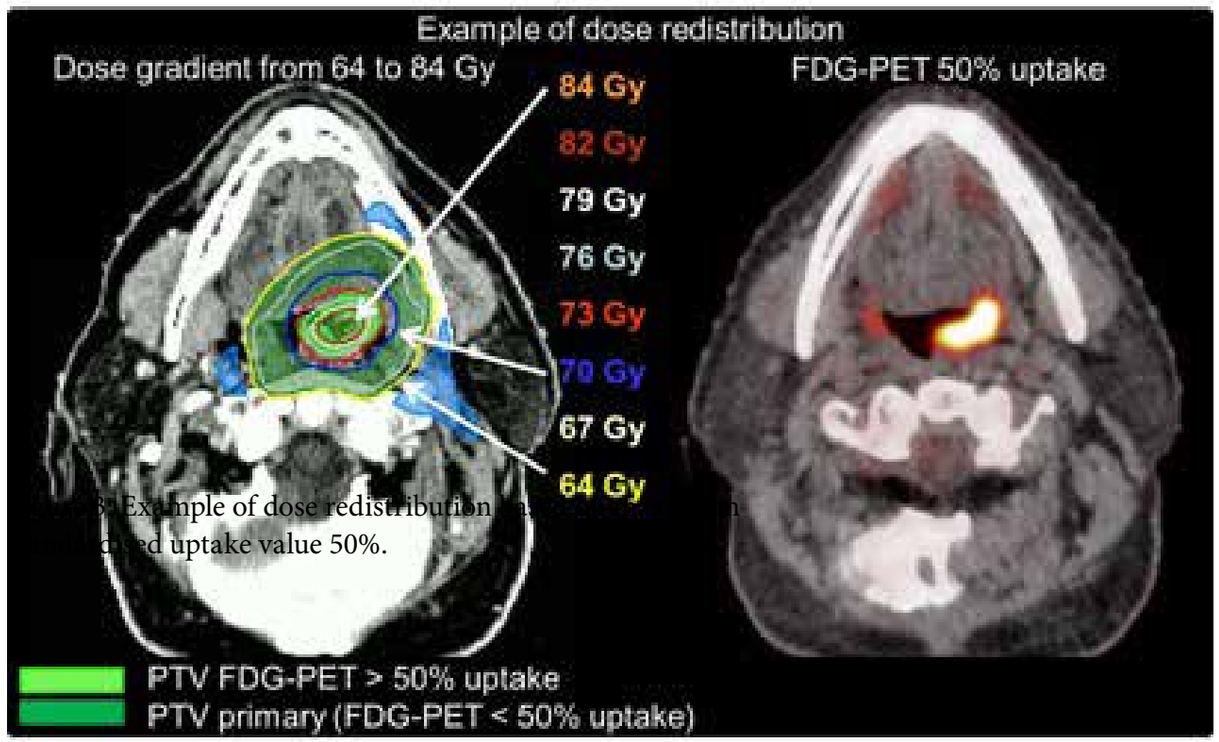
Head and neck dose redistribution trial

Olga Hamming-Vrieze

This trial is aimed at exploring whether radiation dose redistribution improves local control without increased toxicity for patients with squamous cell carcinoma of the oropharynx, hypopharynx or oral cavity; stage III-IV: T3-4, any N, M0. A standard radiation dose to the primary tumour of 70 Gy in 35 fractions is compared to dose redistribution 64-84 Gy in 35 fractions based on FDG-PET uptake with adaptive radiotherapy. Both schedules are given in seven weeks and all patients receive three weekly cisplatin 100mg/m^2 (day one, 22, 43). To guarantee consistency between the participating centres, delineation and planning dummy runs were performed.

The trial is well under way; 105 patients have been randomised by now. From the toxicity data it was concluded that these were according to published literature with suspected unexpected serious adverse reactions to date.

ClinicalTrials.gov Identifier: NCT01504815



Example of dose redistribution [illegible] uptake value 50%.

Adaptive and innovative Radiation Treatment FOR improving Cancer treatment outcomE (ARTFORCE); a randomised controlled phase II trial for individualised treatment of head and neck cancer

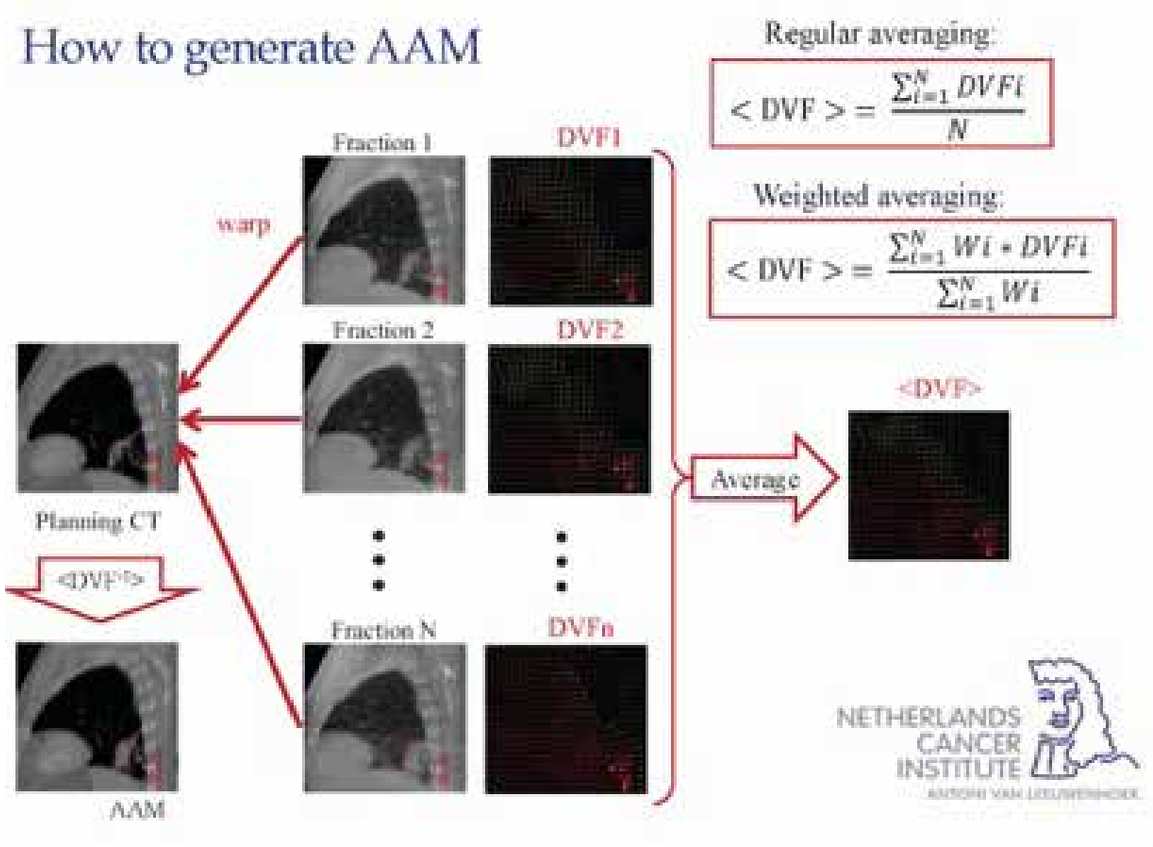
Heukelom J, Hamming O, Bartelink H, Hoebers F, Giralt J, Herlestam T, Verheij M, van den Brekel M, Vogel W, Slevin N, Deutsch E, Sonke JJ, Lambin P, Rasch, C *BMC Cancer*. 2013 Feb 22;13:84

RESEARCH SUPPORTING CLINICAL TRIALS

Adaptive radiotherapy to account for anatomical changes

Jan-Jakob Sonke

Average anatomy modelling (AAM) was developed and validated for lung cancer patients. The aim was to mitigate geometrical uncertainties in adaptive radiotherapy process for repeated CT-scans during treatment. These repeated CT-scans during radiotherapy require extra workload and each CT-scan is just a new snapshot of the patient anatomy. The AAM is therefore a substitute for repeated CTs during radiotherapy, and reduces the workload.



Biological adaptive treatment planning

Iuliana Toma-Dasu, Marta Lazzeroni

The aim of this part of the project is a search for an optimal time point for assessment of the tumour responsiveness to radiation based on repeated FDG-PET images. The method was developed by Toma-Dasu *et al.* (2015) and applied to lung cancer patients, and its feasibility tested on head and neck cancer patients (Figure 4).

The optimal time point for assessment of the tumour responsiveness to the radiation was found to be the second week instead of the third week of treatment and is therefore a better time point. With this approach patients could be stratified as responders versus non-responders. Also dose plans could be developed for adaption of the radiation dose distribution to the radio-resistant areas (Figure 5).

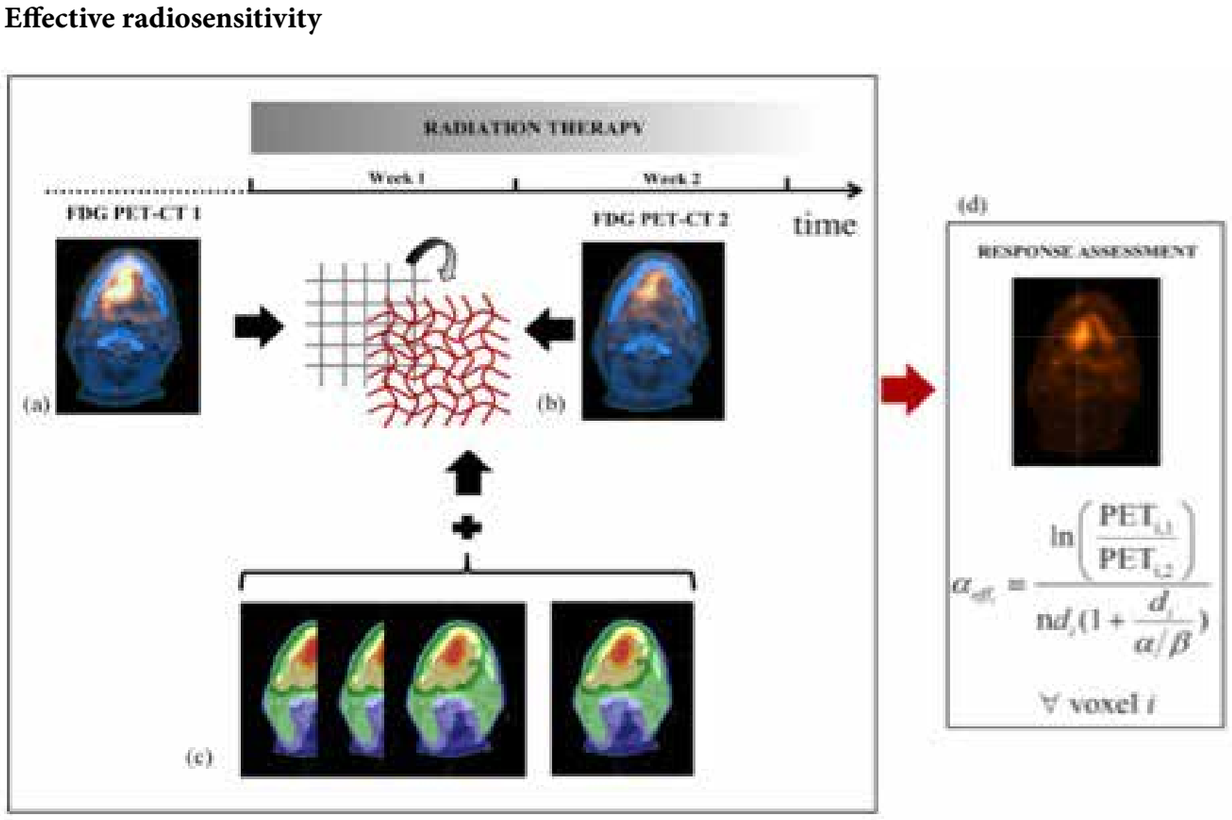


Figure 4: Estimation of the effective radiosensitivity with repeated PET-CT scans

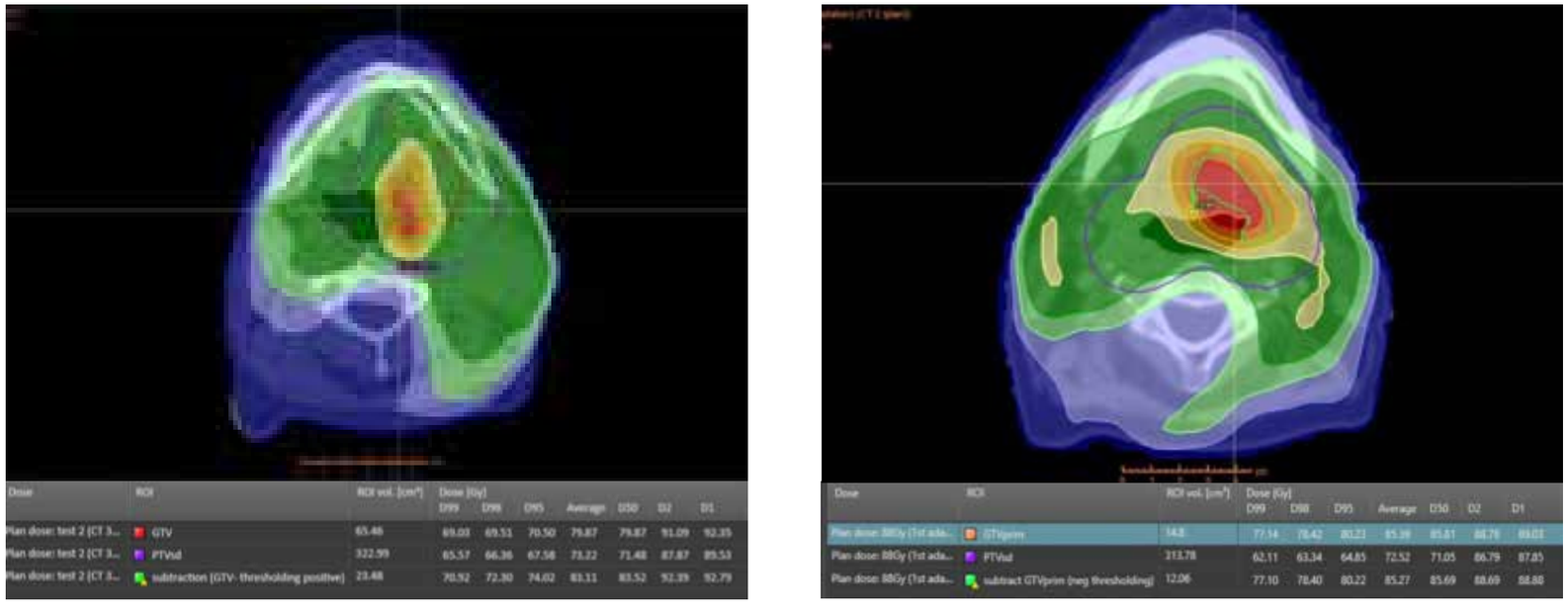


Figure 5: Examples of adapted plans for two patients predicted as poor responders

Evaluating tumour response of non-small cell lung cancer patients with ^{18}F-fludeoxyglucose positron emission tomography: potential for treatment individualization
Toma-Dasu I, Uhrdin J, Lazzeroni M, Carvalho S, van Elmpt W, Lambin P, Dasu A.
Int J Radiat Oncol Biol Phys. 2015 Feb 1;91(2):376-84. doi: 10.1016/j.ijrobp.2014.10.012.

In vivo dosimetry for patient specific clinical trial quality assurance

Wouter van Elmpt

In vivo dosimetry based on cone beam CTs and electronic portal imaging device (EPID) dosimetry was developed for all centres in this project, both for the Varian and the Elekta linear accelerators (Figure 6). The software was installed onsite and calibrated to guarantee treatment delivery in the participating centres. The software allows for a pre-treatment quality assurance procedure inside the planning CT scan that reconstructs the dose to be delivered in a dummy run prior to the first patient irradiation. Also an *in vivo* verification of the delivered dose inside the patient is estimated based on the cone-beam CT scan and the measured exit-dose using EPID dosimetry. This allows for a true delivered dose verification to guarantee treatment delivery of the patients in the clinical trials of ARTFORCE.

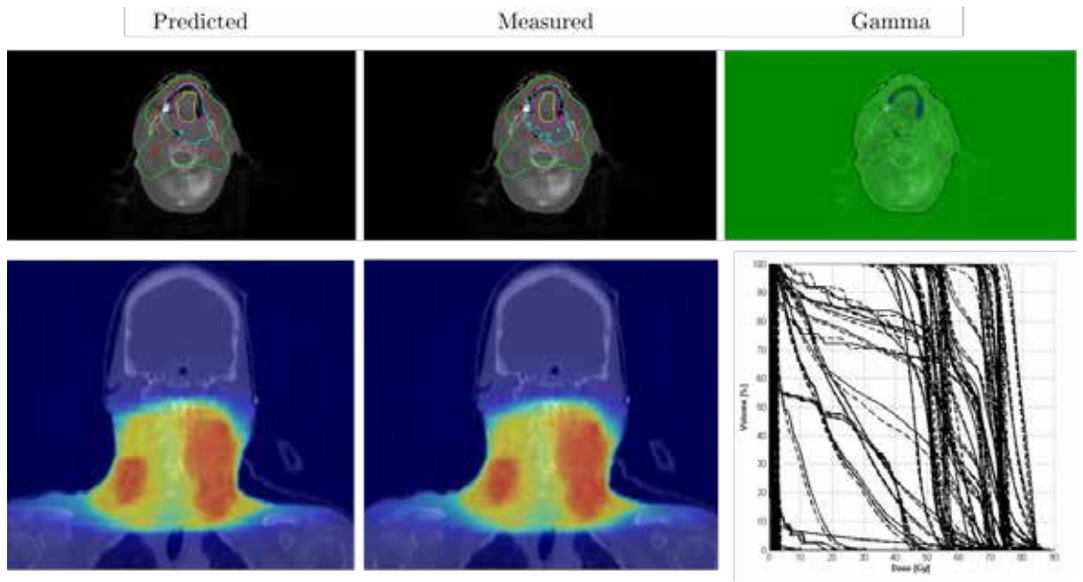


Figure 6: 3D dose reconstruction and verification of the measurement on-site for a head and neck cancer patient treated in the ARTFORCE clinical head and neck trial

Evaluating tumour response of non-small cell lung cancer patients with ^{18}F-fludeoxyglucose positron emission tomography: potential for treatment individualisation
Toma-Dasu I, Uhrdin J, Lazzeroni M, Carvalho S, van Elmpt W, Lambin P, Dasu A.
Int J Radiat Oncol Biol Phys. 2015 Feb 1;91(2):376-84. doi: 10.1016/j.ijrobp.2014.10.012.

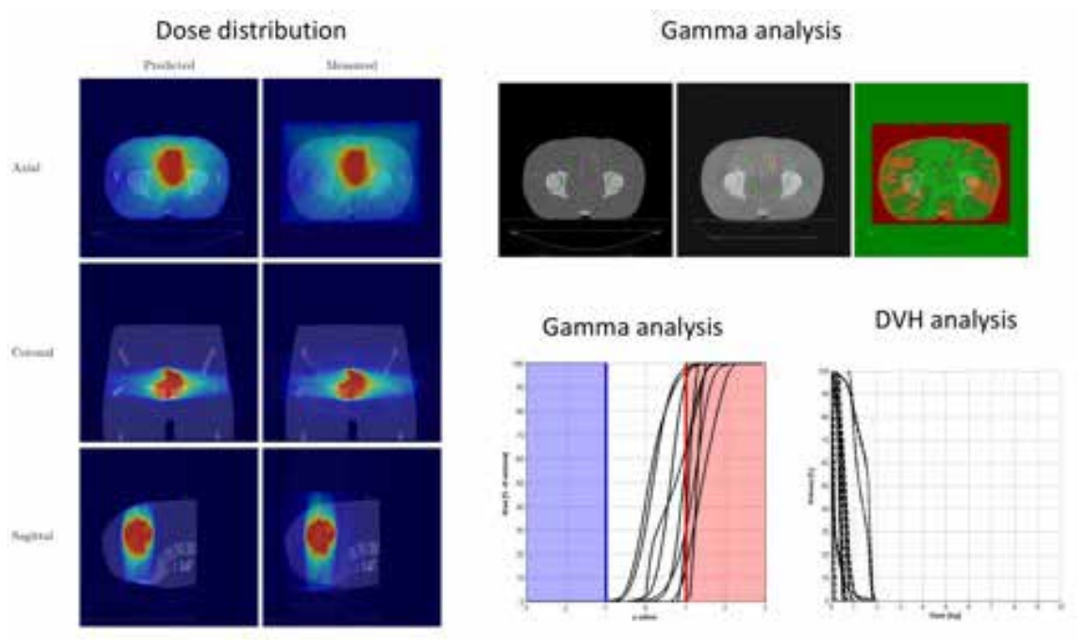


Figure 6:
3D dose reconstruction and verification of the measurement on-site

Three dimensional *in vivo* dosimetry software 3D *in vivo* dosimetry using megavoltage cone-beam CT and EPID dosimetry.
van Elmpt W, Nijsten S, Petit S, Mijnheer B, Lambin P, Dekker A.
Int J Radiat Oncol Biol Phys. 2009 Apr 1;73(5):1580-7.

Online 3D EPID-based dose verification: Proof of concept
Spreeuw H, Rozendaal R, Olaciregui-Ruiz I, González P, Mans A, Mijnheer B, van Herk M.
Med Phys. 2016 Jul;43(7):3969.

Biomarkers for response prediction

Dan Ou, Yungan Tao, Eric Deutsch

Interesting new data were presented on the exploration of the prognostic / predictive value of radiomics in locally advanced head and neck squamous cell carcinoma (HNSCC) patients treated with chemo-radiotherapy (CRT; cisplatin) or bioradiotherapy (BRT; cetuximab) indicating that prognostic radiomics features and p16 could be complementary variables for predicting survival. The long-term results suggested better outcomes in locally advanced HNSCC patients receiving concurrent cisplatin over cetuximab regardless of HPV / p16 status.

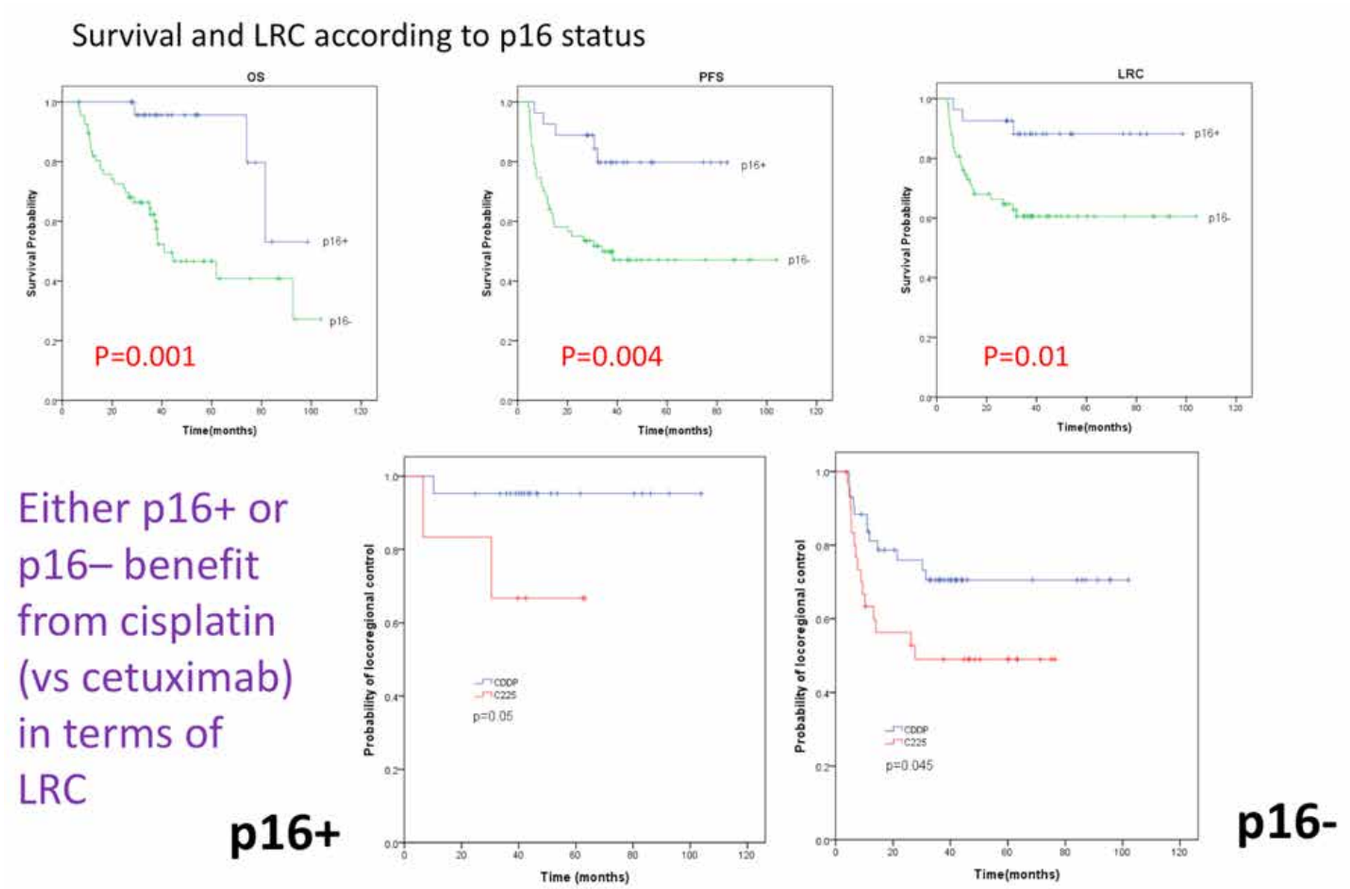


Figure 7: The prognostic but not predictive role of HPV / p16

Further research is aimed at the correlation of immune-biomarkers (PD-L1, CD8, macrophages, etc.) with clinical-pathological parameters and radiomics, and also finding out the potential predictive value of certain radiomics features and immune-biomarkers.

Concurrent chemoradiotherapy with cisplatin or cetuximab for locally advanced head and neck squamous cell carcinomas: Does human papilloma virus play a role?
Ou D, Levy A, Blanchard P, Nguyen F, Garberis I, Casiraghi O, Scoazec JY, Janot F, Temam S, Deutsch E, Tao Y .
Oral Oncol. 2016 Aug;59:50-7.

Molecular imaging and radiomics

Philippe Lambin

The prognostic value of tumour hypoxia and the pattern of relapse with HX4 PET in head and neck, and lung cancer patients was explored prospectively. It seems HX4 is the best imaging biomarker of hypoxia. Furthermore quantitative data from standard imaging to generate quantitative clinically relevant information with the so-called 'radiomics' approach, were extracted. The CT-based radiomics signatures consisting of highly reproducible features linked to tumour heterogeneity and proliferation, and built on lung cancer data, appear to have strong prognostic power in independent datasets of lung and head and neck cancer patients. It has been demonstrated that data from Cone beam CTs could be used for this radiomics approach.

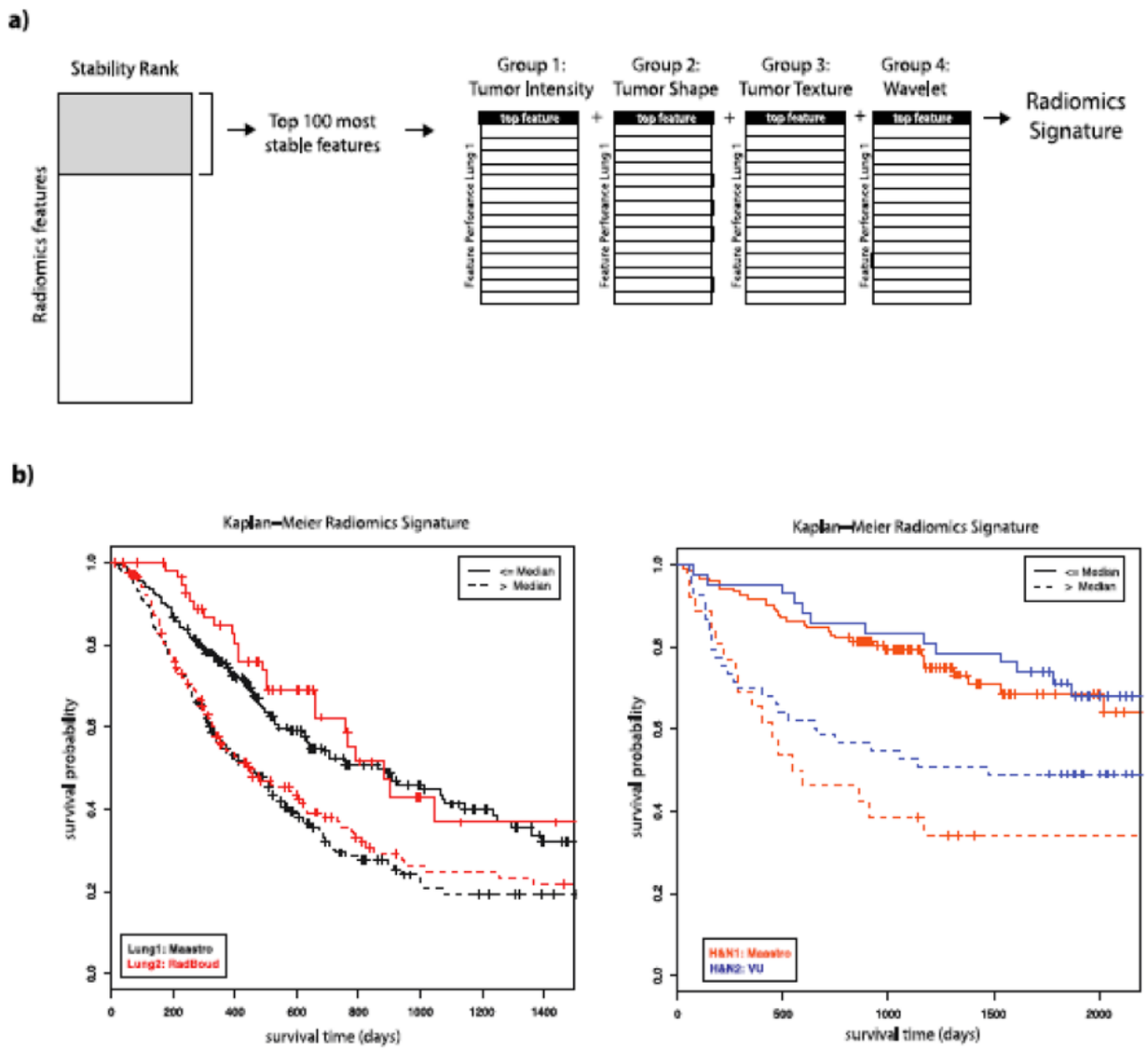


Figure 8: Prognostic performance and gene-expression association of the radiomics signature

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[2] Valuation of tumour hypoxia during radiotherapy using [18F]HX4 PET imaging and blood biomarkers in patients with head and neck cancer. Zegers CM, Hoebers FJ, van Elmpt W, Bons JA, Öllers MC, Troost EG, Eekers D, Balmaekers L, Arts-Pechtold M, Mottaghy FM, Lambin P. *Eur J Nucl Med Mol Imaging.* 2016 Jun 1

[3] Radiotherapy combined with the immunocytokine L19-IL2 provides long-lasting antitumor effects. Zegers CM, Rekers NH, Quaden DH, Lieuwes NG, Yaromina A, Germeraad WT, Wieten L, Biessen EA, Boon L, Neri D, Troost EG, Dubois LJ, Lambin P. *Clin Cancer Res.* 2015 Mar 1;21(5):1151-60.

[4] Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach Hugo J. W. L. Aerts, Emmanuel Rios Velazquez, Ralph T. H. Leijenaar, Chintan Parmar, Patrick Grossmann, Sara Carvalho,Jo han Bussink,René Monshouwer,Benjamin Haibe-Kains,Derek Rietveld, Frank Hoebers, Michelle M. Rietbergen, C. René Leemans, Andre Dekker, John Quackenbush, Robert J. Gillies& Philippe Lambin, *Nature Communications Nat Commun.* 2014 Jun 3;5:4006.