

# ART Appreciation at MAASTRO

Arno Muijtjens

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# ART Appreciation at MAASTRO

At the University of Maastricht, situated in Maastricht, The Netherlands, adaptive radiotherapy is proving to be the key to more precise and effective treatment of tumors.

*By Arno Muijtjens, PhD*

MAASTRO clinic recently moved from the hills of Heerlen to the valley of the Maas River. The new location of the clinic is in the direct vicinity of the Medical Faculty of the University of Maastricht and the Academic Hospital Maastricht, thus stimulating cooperation and integration of the clinic's activities with the two academic institutes. Within the past five years, MAASTRO clinic has evolved from an institute aimed at routine patient care to an institute combining care with research and education at an academic level. "We were expanding and extended our staff, aiming at the enforcement of our research potential, but we were happy to see that we also succeeded in involving part of our radiation technologists in research – and three of them started a PhD project," says Loes Klaasse-van Remortel, Managing Director of MAASTRO clinic. Klaasse-van Remortel explains that with the new housing and equipment, the clinic is ready for the future. Additionally, the architect succeeded in creating a light-filled, friendly atmosphere in the building, which benefits the patients as well as the more than 200 staff members working at MAASTRO clinic. The clinic currently houses five Siemens ONCOR® linear accelerators, which will be increased to six in early 2007, with room left for a seventh linac to complete the equipment for radiotherapy. In addition, for diagnostic purposes and radiotherapeutic planning, MAASTRO clinic is equipped with a PET·CT scanner, a large-diameter computed tomography (CT) scanner, and a regular CT scanner.

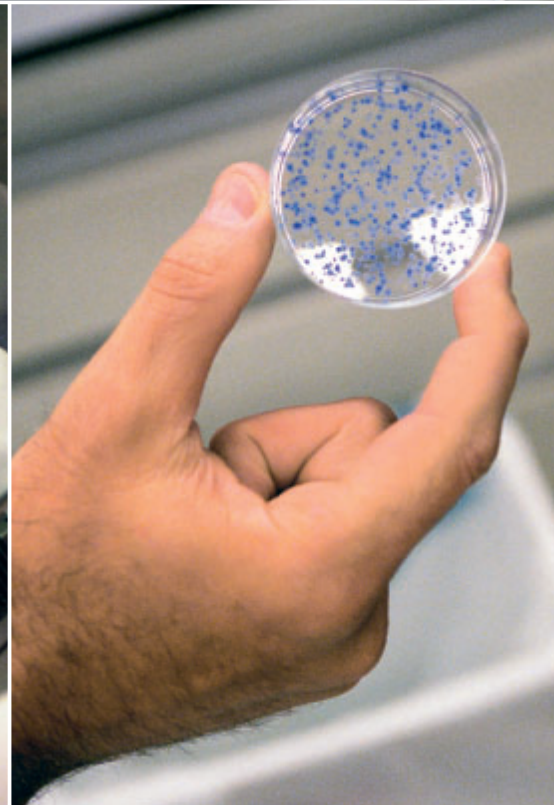
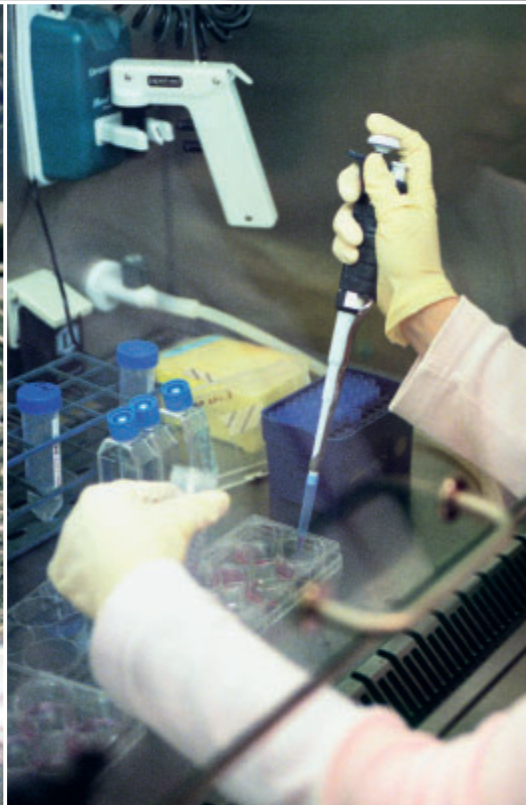
"MAASTRO clinic and Siemens have been cooperating for five years," Klaasse-van Remortel explains, "and it has been a pleasant and successful experience, as indicated by the

many promising research projects." MAASTRO clinic and Siemens set up a collaborative meeting each year to evaluate the activities of the past year and plan new projects for the following year. Then MAASTRO's research activities and Siemens contributions to the projects are defined. "This cooperation," Klaasse-van Remortel emphasizes, "has proven to be a typical example of a 'one-plus-one-equals-three' experience. Siemens shares our strategic vision and is prepared to participate in the investment. Our cooperation turned out to be a good decision."

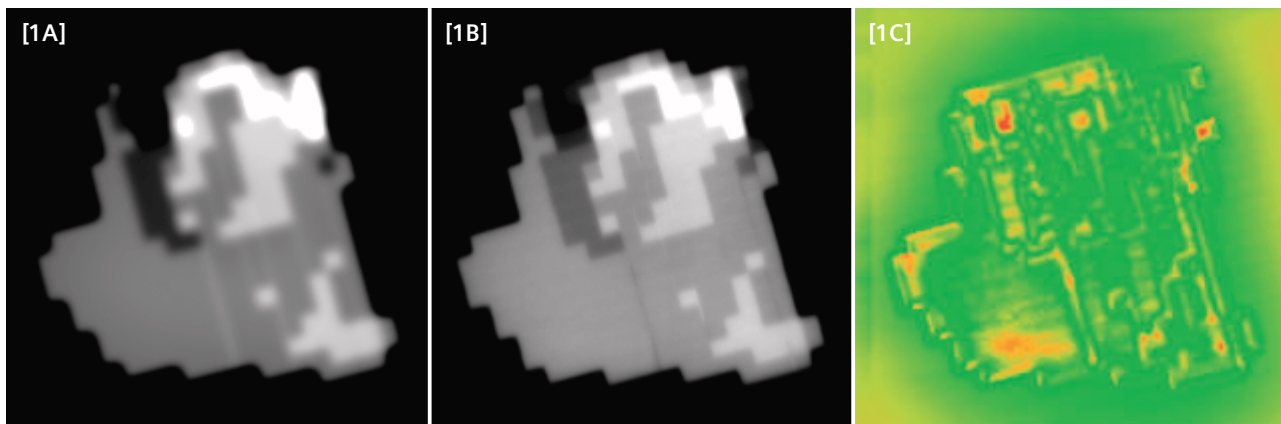
## Full Integration Optimizes ART

"MAASTRO was one of the first institutes worldwide to be provided with a PET·CT simulator," reports Professor Philippe Lambin, MD, Medical Director of MAASTRO clinic and Professor at the University of Maastricht. "It has offered us the opportunity to develop methods to obtain more accurate information about the type, shape, and location of tumors, as well as to develop new methods of optimizing radiation therapy. In lung cancer, we moved to irradiation of PET-positive areas, and the corresponding increase in accuracy enabled us to reduce the target volume and increase the dose. In the next step, we moved from aiming at fixed dose to aiming at fixed toxicity in therapy planning, thereby increasing the probability of cure."

Using respiratory correlated PET·CT images, Lambin and his team were able to improve the estimation of moving tumor volume. Basing the irradiation plan on this information, they were able to considerably reduce the probability of missing



IN THE PAST FIVE YEARS, MASTRO clinic has evolved to an institute combining patient care with research and education at an academic level. With equipment like PET-CT, gene arrays, and the new Biobank, the clinic is ready for the future.



[1] The dose delivery by complex intensity modulated radiation therapy (IMRT) treatments can be verified by using the Siemens OptiVue™ amorphous silicon EPID. For each intensity modulated treatment field, a portal dose distribution can be predicted using the beam parameters [1A], and measured using the EPID [1B] without a patient in the beam (pretreatment verification). From the two dose distributions, a so-called Gamma function distribution can be derived [1C]. Gamma function values can be used to determine if differences in both dose and distance are within specified tolerance (green/orange) or not (orange/red).

parts of the tumor during treatment while minimizing the amount of normal tissues that is irradiated. Delineation of the tumor by image-analyzing techniques instead of manual procedure further improved accuracy and precision of the measured tumor volume, as results in trials have shown. “Application and further development of adaptive radiotherapy have enabled us to correct for changes in tumor volume and location during treatment,” says Lambin.

Using adaptive radiotherapy (ART), the changes in position and volume can be detected just before treatment through analysis of portal images obtained with the Siemens MVision™ Megavoltage Cone Beam Imaging package, thus enabling soft tissue imaging. The differences found between diagnostic and treatment images are used to correct therapy and dose planning by adjusting them to the location and volume of the tumor at the time of treatment. Thus, ART enables more precise and more effective radiotherapy.

Lambin points out the cooperative aspects of his relationship with Siemens: “They provide us with the latest beta versions of their hardware and software, enabling MAASTRO clinic to perform research and publish the results. Siemens subsequently learns from these early user experiences and obtains information about points for adjustment or improvement.” For adaptive radiotherapy, Siemens provided MAASTRO clinic with the ONCOR linac with MVision, the SOMATOM® Sensation Open with a laser system as part of the VolumesIM simulation, the verify-and-record system LANTIS®, and a set of COHERENCE™ workspaces. Through this setup, adaptive targeting is fully integrated into the radiotherapy procedure. Medical physicist Bas Nijsten, MSc, adds, “We also employ

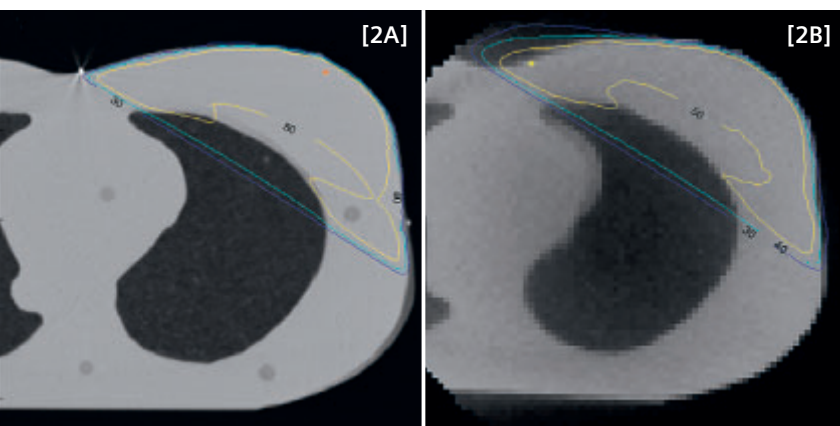
the available portal imaging facilities for portal dosimetry. Therefore, we can advance from radiotherapeutic dosage plans based on predictions to plans based on in vivo dose measurements. The additional feedback further increases the precision, and thereby the quality, of the treatment. At the moment, we are using 2D dose information, but we are heading for the development of accurate 3D in vivo dose reconstruction.”

## The Role of the Biobank

“We have managed to move to the academic level in the last five years, setting up the required research and educational infrastructure,” says Klaasse-van Remortel. “Our ambition for the next five years is the development of individualized treatment, aiming at higher survival, fewer complications, and improved cost efficiency.”

Lambin asks the obvious question and then proceeds to answer it: “How can we provide individualized treatment? The broader context of the problem consists of three aspects: the molecular, the biological, and the imaging aspect. We must develop methods to use all available information to optimize the choice of treatment.”

For one tumor type, there may be ten or more possible treatments. It is far too complex for a doctor to integrate all the available information and reach an optimum choice of treatment. But combining the molecular, biological, and imaging data in a database creates information that can be seen as a tumor passport. Molecular data is important, because it may be predictive for the sensitivity to treatment, the tolerance to radiotherapy, and other factors.



[2] In radiotherapy, an individual treatment plan is generated per patient, resulting in a predicted 3D dose distribution inside a patient [2A].

Usually, a kilovoltage CT scan is used to localize tumor and normal tissues, and to feed the dose calculation engine with electron densities. To verify the dose delivery, portal dose distributions measured pretreatment with an EPID can be used in a 3D dose reconstruction algorithm to calculate the 3D dose distribution inside a patient [2B].

Variations in patient anatomy can be accounted for by using a CT scan made prior to treatment with the Siemens OptiVue EPID (a Megavoltage Cone Beam scan). In this case, a lung phantom is used, and a Monte Carlo dose calculation engine for the 3D dose reconstruction. The predicted and measured 3D dose distributions agree very well.

“To illustrate this,” says Lambin, “consider a phenomenon called gene polymorphism – the status of genes in normal tissue. For some of these small, normal variations, we have indications that they are associated with an individual’s chance to develop lung complications or not.” Storing this kind of molecular information in a database and learning about the associations with the development of disease and the response to treatment is intended to optimize an individual patient’s treatment. “We can therefore operate on an intermediate level between diagnosis and treatment, the so-called theragnostic level, which supports tailoring a treatment to an individual patient. In addition to molecular, biological, and imaging data, clinical data and quality of treatment data are also stored in the database, which we call Biobank.”

Nijsten adds, “All images obtained in clinical routine are stored in a DICOM database and will also be part of the Biobank, as well as all data in the electronic patient record system.”

Molecular imaging information obtained with PET-CT is validated on the basis of correlation studies comparing results of pathologic analysis of biopsies with the PET-CT imaging data. These activities are aimed at obtaining gene signatures, such as those for hypoxia, and proliferation that help to improve the prediction of prognosis and treatment.

Using the information in the Biobank as a learning set, by applying machine learning methods, a data-based prediction of a patient’s diagnosis, prognosis, and best treatment can be obtained.

The Biobank is set up in a cross-institutional cooperation of MAASTRO clinic with other institutes in the University of

## What is Adaptive Radiotherapy?

Adaptive radiotherapy (ART) enables the therapist to detect and react to changes in positioning, shape and activity of a tumor at treatment time.

Standard procedure is that, based on diagnostic 3D imaging, the target volume is defined, and radiotherapy is planned for a patient over a period of several weeks. However, at the time of treatment, the target volume may have moved, or its shape may have changed. The patient’s position may be different due to voluntary movement, or the tumor location may be different due to motion associated with respiration or digestion. Also, shape and size of the tumour may change during treatment, as well as shape and size of adjacent organs. With the development of the MVision Megavoltage Cone Beam for clinical use, the therapist is provided with a tool to obtain images at treatment time. By comparing the latest 3D imaging information with the earlier obtained diagnostic imaging information, differences can be detected and measures can be taken, for example altering the patient’s position, adapting the target volume, or adjusting therapy and dose planning. Thus, adaptive radiotherapy enables more accurate and more effective radiotherapy, thereby improving patient care.

Maastricht (research institute GROW), Liège, Genk, and Hasselt (Belgium). Currently, the Biobank contains the data of 1,000 patients from MAASTRO clinic. Large amounts of data are required to develop the machine learning model's structure and obtain accurate parameter estimates. In addition, an independent test set of data is needed to validate the learning results. As the content of the database increases in quantity and quality, the learning process will proceed – and as a result, the quality of the predictions is expected to further improve.

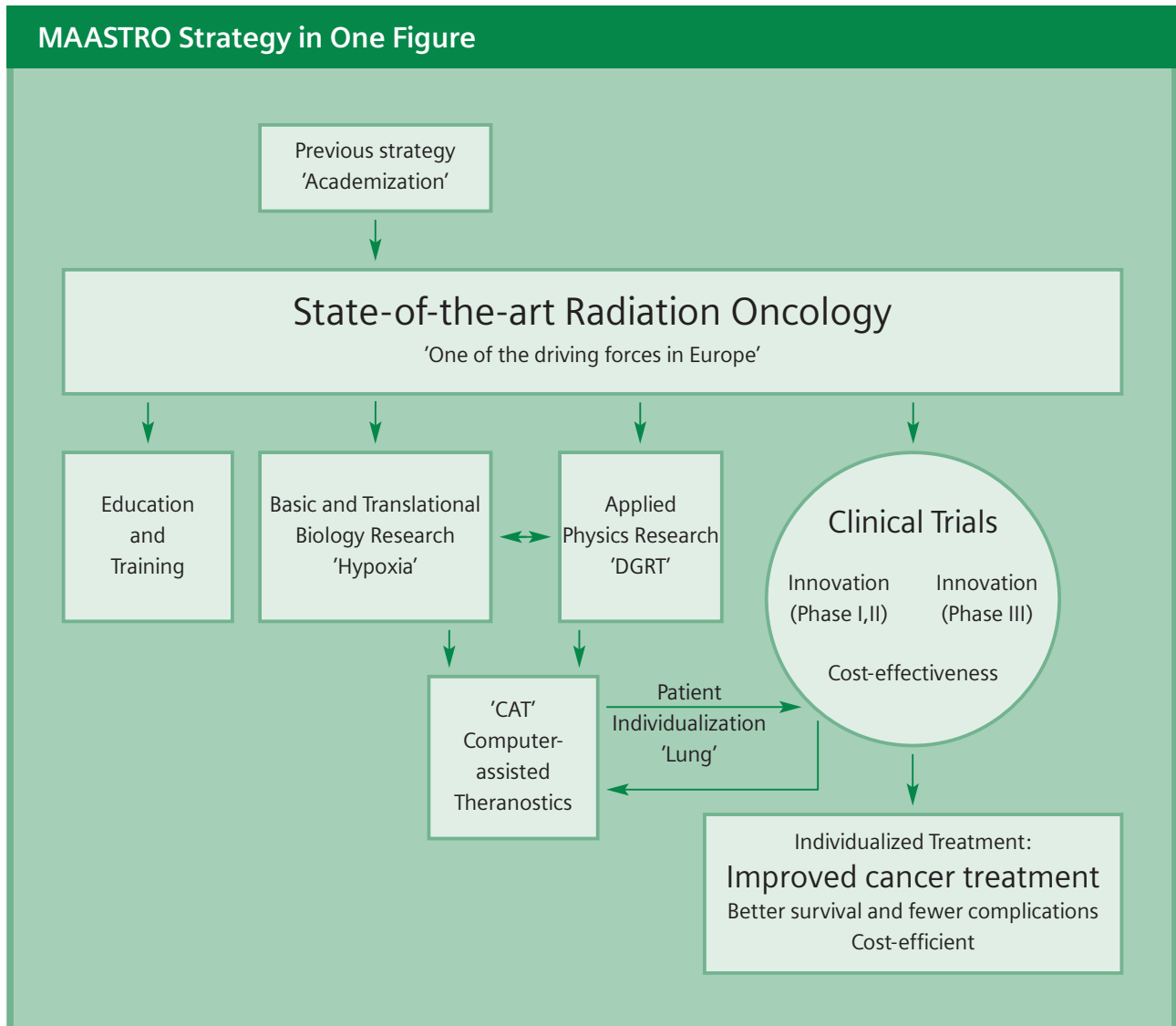
MAASTRO clinic developed this concept of computer-assisted theragnostics (CAT) in a collaborative project with Siemens Computer-Aided Diagnosis and Knowledge Solutions group. The members of this group provide the required expertise

in the fields of machine learning, data-mining methods, and software.

MAASTRO clinic is primarily aiming at the development of a CAT system for lung cancer. Accordingly, the research activities in the next five years will be focused on three major subjects: predictive models for the effects of treatment of lung cancer, dose-guided radiotherapy (DGRT), and tumor hypoxia.

MAASTRO clinic cares for cancer patients today and researches promising new treatment options for tomorrow.

**Author:** Arno Muijtjens, PhD, is Assistant Professor in the Department of Educational Development and Research at the University of Maastricht, The Netherlands. He has contributed his expertise in the technical aspects of medical R&D to a number of international scientific journals.





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Loes Klaasse-van Remortel,  
Managing Director, MAASTRO clinic,  
Maastricht, The Netherlands



»All images obtained in clinical routine are stored in a DICOM database and will also be part of the Biobank.«

Bas Nijsten, MSc,  
Medical Physicist, MAASTRO clinic,  
Maastricht, The Netherlands



»With PET-CT we develop new methods of optimizing radiation therapy.«

Philippe Lambin, MD,  
Professor and Chairman,  
Department of Radiation Oncology,  
Medical Director, MAASTRO clinic,  
Maastricht, The Netherlands

SHARING A STRATEGIC VISION with Siemens – and a pleasant and successful cooperation: Loes Klaasse-van Remortel, Bas Nijsten and Philippe Lambin (from top to bottom).

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