



FINAL PUBLISHABLE JRP REPORT

JRP-Contract number	HLT09	
JRP short name	MetrExtRT	
JRP full title	Metrology for Radiotherapy using Complex radiation Fields	
Version numbers of latest contracted Annex Ia and Annex Ib against which the assessment will be made	Annex Ia:	V1.1
	Annex Ib:	V1.1
Period covered (dates)	From 1 June 2012	To 31 May 2015
JRP-Coordinator	Jean Marc Bordy, Dr, CEA Tel: +33 1 69 08 41 89 Email: jean-marc.bordy@cea.fr	
JRP website address	http://radiotherapy-emrp.eu	
Other JRP-Partners	JRP-Partner 1 CEA, France	
	JRP-Partner 2 CMI, Czech Republic	
	JRP-Partner 3 ENEA, Italy	
	JRP-Partner 4 MKEH, Hungary	
	JRP-Partner 5 NPL, United Kingdom	
	JRP-Partner 6 PTB, Germany	
	JRP-Partner 7 SMU, Slovakia	
	JRP-Partner 8 STUK, Finland	
	JRP-Partner 9 VSL, Netherland	
	JRP-Partner 10 DTU, Demark	
REG-Researcher (associated Home Organisation)	Veronique Dedieu UdA, France	01 March 2013 24 months
	Giuseppe Prestopino UniTov, Italy	01 November 2013 12 months

Report Status: PU Public





TABLE OF CONTENTS

1	Executive Summary	3
2	Project context, rationale and objectives.....	4
3	Research results	6
4	Actual and potential impact	15
5	Website address and contact details	16
6	List of publications.....	16

1 Executive Summary

Introduction

Advances in technology have enabled the introduction of new, complex forms of radiotherapy for the treatment of cancer, including different energies, particles, beam widths and scanning techniques. The doses and delivery methods are often far removed from established reference dosimetry conditions and standards. While the tissue being targeted for treatment may be well defined to reduce damage to surrounding healthy tissue, the accuracy with which the dose is delivered may fall short of the requirements given by ICRU (International Commission on Radiation units and Measurements). The project developed primary standards and good practice guidelines to improve the accuracy of dose measurements made in a clinical setting, enabling clinicians to demonstrate that the delivered dose matches the planned treatment.

The Problem

Modern radiotherapy treatments aim to deliver the appropriate dose to the tumour to kill the cancer cells while saving the surrounding healthy tissue. This is achieved using complex radiation fields that deliver intense radioactive doses to areas of only a few millimeters across, or via brachytherapy where the radiation source is placed inside the body as close as possible to the tumour. Too low a dose in the target volume increases the risk of treatment failure through recurrence of the cancer, while too high a dose can result in higher incidence of severe side effects.

Today, in modern photon radiotherapy dose accuracies of about 8 % can be achieved, but in high-energy photon, electron and particle therapy the accuracy is much lower. The project aimed to address the urgent need for further advancements in dosimetry in radiotherapy and improve methods to bridge the gap between the high-level reference standards and clinical conditions. This current lack of traceability to established reference dosimetry and primary standards makes it more difficult to meet the requirement of ICRU Report 24.

The absorbed dose to water is the basic quantity in dosimetry for radiation therapy. Whilst absorbed dose to water based protocols are widely used for reference dosimetry for high energy photons, this is not the case for other radiotherapy modalities such as low and medium energy x-rays. Particle beam dosimetry is based on calibrations in high-energy photon beams and using correction factors for the difference in beam quality, this combination has a considerable uncertainty. Direct calibrations in terms of absorbed dose to water are not available for scanned ion beams but, in principle, can be derived for other radiation types and the associated correction factors.

The Solution

The MetrExtRT project produced:

1. New references in terms of absorbed dose to water for medium x-ray energies.
2. New integral quantities for the characterisation of high energy x-rays for SRS and SRT (stereotactic radiosurgery and radiotherapy) and IMRT (imaging modulated radiotherapy).
3. Improved consistency and traceability of proton and carbon ion beams, in particular novel types such as scanned particle beams.
4. A traceable measurement system for the verification of dose and distribution in complex radiation fields for the verification of treatment planning systems (TPS).
5. A metrological chain, from the primary standard to the end user's calibration and treatment verification, for the use of low energy x-rays for brachytherapy.

Impact

The project developed methodologies, primary standards and guidance for new complex radiation treatments. The results of the project will have significant effect of future technology for radiation treatment. The work has contributed to the research on radiation metrology, and reflects the continuous evolution of the modalities and complexities of treatments.

2 Project context, rationale and objectives

The need for effective radiotherapy is demonstrated by the fact that there are 4 million new cases of cancer in Europe per year. These figures are predicted to increase in the future due to the improvement of diagnostic methods and the global ageing of the population in Europe. About 75 % of cases are treated using radiotherapy (alone or with chemotherapy and/or surgery), and it is estimated that about 50 % of successful treatments can be attributed to radiotherapy.

The lowest uncertainties are required for radiotherapy since the goal of radiotherapy is to kill the tumour cells and simultaneously achieve a high survival rate of the surrounding healthy tissue. In the dose range over which the effect on tumour cells varies most rapidly a change of the dose by 5 % can result in a change of the tumour control probability of 50 % and can result in a normal tissue complication probability of 20 % to 30 %. Today, in modern photon radiotherapy uncertainties of about 8 % can be achieved, in high-energy photon, electron and hadron therapy and brachytherapy the uncertainties are up to 20 %. These figures are far from the requirements of the International Commission on Radiation Units and Measurements of a standard uncertainty for the dose applied to the tumour of less than 2.5 % for teletherapy, and less than 5 % for brachytherapy. These discrepancies emphasise the urgent need for further advancements in dosimetry in radiotherapy in terms of (i) absorbed dose to water standards for low and medium energy X-rays, (ii) accuracy for radiation beams smaller than 2 cm x 2 cm by applying correction factors to the absorbed dose at a point or by introducing an integral quantity and (iii) dose to the tumour traceability through calibration of transfer dosimeters and treatment quality control methods and updated codes of practice for clinical reference dosimetry.

From the regulation point of view, EU Directive 97/43/EURATOM is now widely interpreted as making in-vivo dosimetry mandatory for all radiotherapy patients. Commonly used existing systems have the undesirable features that additional time is needed to attach the detectors, that only skin dose can be verified directly, that point dose information can be hard to interpret in relation to a complex planned dose distribution, that realistic tolerances can only identify gross errors and, in practice, users find that out-of-tolerance measurements are most often accounted for by an error in positioning the dosimeter. Such features make the benefit of such an in-vivo dosimetry system marginal at best. The lack of convenient and effective in-vivo dosimetry systems has contributed to an increased risk of error in patient treatment, with a consequent reduction in therapeutic efficacy and patient safety.

Radiotherapy metrology can be characterised by at least 4 main features, (i) the relatively high standard uncertainty associated with the best metrological standards available (of the order 0.5 %) compared to the need to achieve a standard uncertainty of 2.5 % in the dose applied to the tumour (ICRU), (ii) the extensive use of software in the treatment process which can introduce large errors in the calculation of the dose distribution in and around the tumour, (iii) the difficulty in tracking the tumour, and (iv) the gap between the reference and the clinical conditions. In order to minimise the uncertainty on the dose and its 3D distribution, it is necessary to work on all the steps of the metrological chain. This means at the NMI to improve the standards in terms of uncertainty and adequacy to the clinical application and at the hospital to have the best tools available to control the dose distribution in and around the tumour

Today, clinical reference dosimetry is based on standards of absorbed dose to water as described in codes of practice such as IAEA TRS-398, AAPM TG-51, IPEM-1990, DIN-6800-2 and NCS Report 18. The main advantages of using the quantity absorbed dose to water as the basis of clinical dosimetry are the avoidance of the use of conversion factors from air kerma (the basis of an earlier generation of codes of practice) and the generally simpler mathematical formalism. Whilst absorbed dose to water based protocols are widely used nowadays for reference dosimetry in high energy photon, electron, proton and ion beams, this is not the case for other radiotherapy modalities such as low and medium energy x-rays. Proton and ion beam dosimetry is based on calibrations in high-energy photon beams requiring correction factors for the difference in beam quality with a considerable uncertainty. Direct calibrations in terms of absorbed dose to water are not available for proton and ion beams but in principle, calorimeters exist that are able to measure direct correction factors for passively scattered hadron beams. In TRS 398, only large radiation beams are used (e.g. 10 cm x 10 cm for high-energy photon beams), which are not representative of the clinical conditions in some modern treatment modalities (such as intensity modulated radiotherapy, stereotactic body radiotherapy and scanned particle beams) where many small beams are combined together from different angles to achieve better conformation of the irradiated volume to the target volume and at the same time providing improved organ at risk sparing. One of the main features of radiotherapy is the extensive use of software in the treatment process to calculate the dose distribution in the patient. This dose calculation

software forms part of the treatment planning system, which, at present, exhibits deficiencies in most implementations which can result in large errors. For photon beams this occurs at interfaces between media where secondary charged particle disequilibrium exists, for electrons this is due to simplifications of the calculation algorithms compared to the real physical interacting processes with matter. For proton and ion beams this is due to the uncertainties in the relation between stopping powers and colour (grey level) of the diagnostic image.

The project had 5 specific scientific and technical objectives:

1. To develop and compare new references in terms of absorbed dose to water for medium x-ray energies. (Before the project there was no direct traceability through the absorbed dose to water measurement.)
2. To study new integral quantities for the characterisation of high energy x-rays for SRS and SRT (stereotactic radiosurgery and radiotherapy) and IMRT (imaging modulated radiotherapy). (The treatment conditions are too far from the reference ones involving rotating beams, and correction factors would lead to high uncertainties).
3. To improve the consistency and traceability of proton and carbon ion beams, in particular novel types such as scanned particle beams. (These heavy charged particles can reach the tumour with smaller dose to the surrounding healthy tissue, but because the beams are narrow they are used in a scanning mode. There are no references for this type of irradiation)
4. To develop a traceable measurement system for the verification of dose and distribution in complex radiation fields for the verification of treatment planning systems (TPS). (This objective looked at high energy radiation)
5. To develop a metrological chain, from the primary standard to the end user's calibration and treatment verification, for the use of low energy x-rays for brachytherapy. (Brachytherapy involves the low energy x-ray tubes being inside the body, and hence closer to a tumour, and again there are no standards for this situation.)

3 Research results

3.1 *To develop and compare new references in terms of absorbed dose to water for medium x-ray energies.*

A new concept of mixed water/graphite calorimeter with sensitive elements immersed in water at 2 cm depth has been developed by ENEA to assess absorbed dose to water at 2 cm depth as required for medium energy X rays in AIEA technical report series n°398 (figure 1) [17]. As the reference medium for radiotherapy is water, MC calculations have been made for an accurate evaluation of factors to convert absorbed dose to graphite into absorbed dose to water. In addition to the ENEA primary standard, there are three other primary references in Europe (at LNE-LNHB, PTB and VSL) based on different measuring device designs such as water calorimetry, allowing their comparison [7].

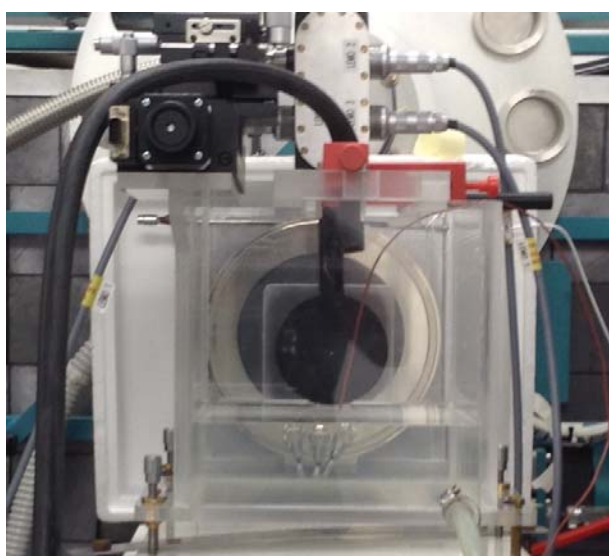


Figure 1: The mixed graphite-water ENEA calorimeter.

Prior to launching a comparison in terms of absorbed dose to water, two inquiries were made. One among the end users to define the radiation qualities used for treatments in radiotherapy services in Europe and one among the European calibration laboratories to know which radiation qualities are used for calibration.

From the end users enquiry, it turns out that the high voltage used for treatment lies between 10 and 250 kV with additional filtration up to 1 mm Cu for 150 kV. The dose rates are between 0.3 and 25 Gy/mn with 80 % below 5 Gy/mn and 10 % below 0.5 Gy/mn. 54 % of the treatments are for contact therapy (e.g. skin, eyes, rectum, genecology) and 11 % for interventional surgery (breath).

Based on the answers to this enquiry, the ratio between the first and second Half Value Layer (HVL) was calculated for all radiation qualities in order to compare the radiation qualities of the end users to the ones used in calibration laboratories. CCRI (Comité Consultatif pour les Rayonnements Ionisants, the main the radiation qualities used for international comparisons) and DIN 6809-5 radiation qualities were found more suitable than the RQR and RQA radio diagnostic taken in IEC standard 61267 and those used in radiation protection taken from ISO series 4037 (figures 2 and 3).

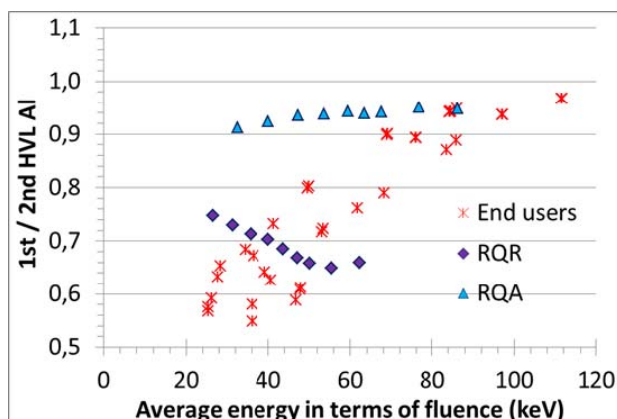


Figure 2: Comparison of the characteristics of the end users and IEC 62167 (RQR and RQA) radiation qualities

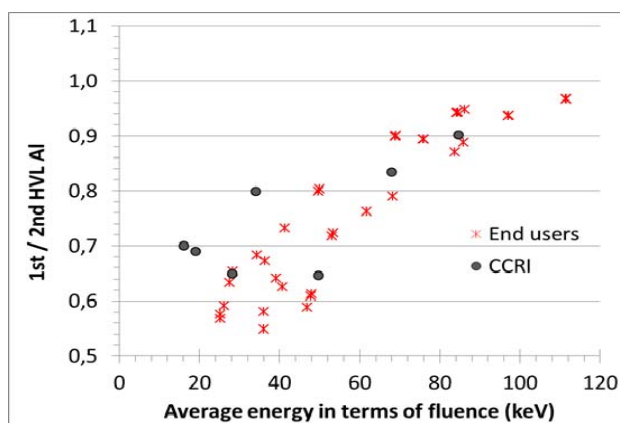


Figure 3: Comparison of the characteristics of the end users and CCRI radiation qualities

The comparison in terms of absorbed dose to water was organised by PTB. Using the selected CCRI and DIN 6809-5 radiation qualities, plane parallel ionisation chambers were calibrated by four laboratories, LNE-LNHB, PTB, VSL and ENEA. The first results showed deviation smaller than $\pm 1\%$ between the laboratories [16]. Another standard based on an extrapolation chamber (figure 4) was greatly improved at MKEH and shall lead to the establishment of a fifth primary standard for medium energy X-ray in Europe.

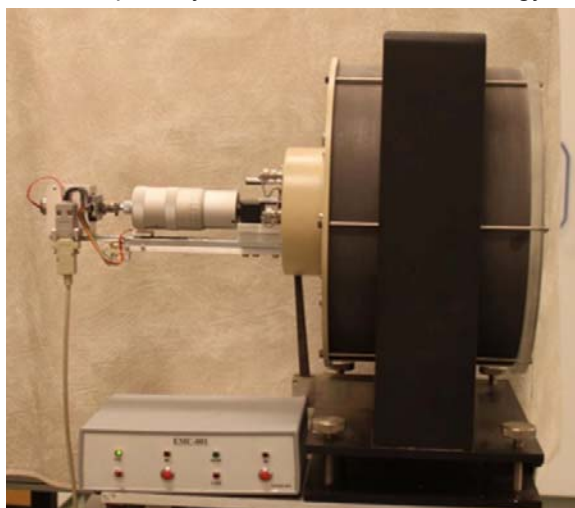


Figure 4: The MKEH extrapolation chamber

3.2 *To study new integral quantities for the characterisation of high energy x-rays for SRS and SRT and IMRT*

In modern radiotherapy, following the introduction of multi-leaf collimators in medical LINACs and of new dedicated treatment facilities such as TomoTherapy and CyberKnife units, the size of the irradiation beams for treatments has decreased drastically, increasing the gap with the calibration beam size defined in international protocols such as IAEA 398. Theoretically, the smallest field size achievable is about 4 mm diameter, in practice it is rare to treat with fields smaller than one cm². The use of small high energy X-ray (above 6 MV) fields in radiotherapy, with sizes below about 2x2 cm², can lead to a lack of lateral electronic equilibrium at the point of measurement at 10 cm depth in water which makes point dose quantity unsuitable. In the case of such very small fields, the first idea is to decrease the size of the sensitive volume of the calorimeter; unfortunately decreasing its size leads to a decrease in sensitivity in such a way that an accurate measurement is no longer possible.

To overcome this difficulty an LNE-LNHB specially designed large area graphite calorimeter (figure 5), named GR11, able to be used in small radiation fields (smaller than 2x2 cm²), similar to those used in SRS and SRT (Stereotactic Radio Surgery and Radio Therapy) and IMRT (Imaging Modulated Radio Therapy), was built and is operational. The design of the calorimeter is the same as for the former graphite calorimeter where graphite bodies (core, jacket and shield) are maintained with void gaps between them by thin nonconductive wires. Thermistors are embedded in the graphite core to measure the increase of temperature. The core is put in the graphite phantom at a depth equivalent to 10 cm in water.

The sensitive area of such a calorimeter is larger than the field dimensions so that it measures the energy deposited by the whole radiation beam and the measured quantity is no longer a dose defined at a point, but a surface quantity similar to a dose area product (DAP). This device allows, for the first time in radio diagnostics, to overcome the lack of electronic equilibrium in small fields [18,19].

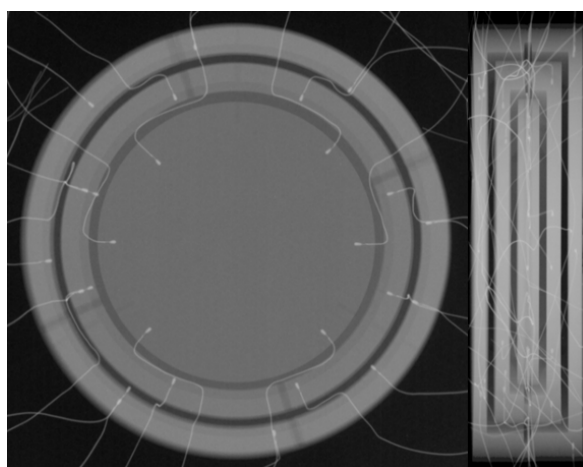


Figure 5: Top and side radiography of the LNE-LNHB graphite calorimeter detector, small white points are thermistors embedded in the graphite core (centre) and in the jacket and the shield surrounding the core.

A comparison was made between the new calorimeter and two existing LNE-LNHB calorimeters with smaller sensitive volumes (diameter 1.6 cm for GR09 and 0.6 cm for GR10) designed to measure point dose quantity in beam size down to 2x2 cm². It shows that the three calorimeter measurements are compatible within one standard uncertainty (figure 6).

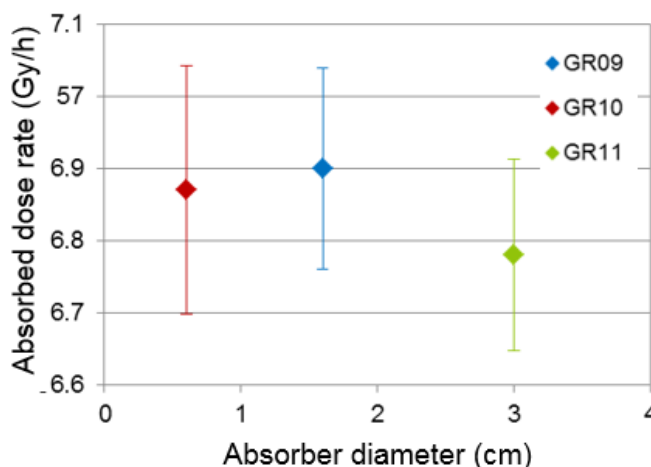


Figure 6: Comparison of graphite calorimeter measurements of absorbed dose to graphite with calorimeter absorber diameter of 1.6 cm (GR09), 0.6 cm (GR10) and 3.0 cm (GR11), error bars show standard uncertainties.

Measurements in small fields down to 0.75 cm of diameter with specially designed collimators show the feasibility of DAP measurements for high energy photons. Transfer standards based on homemade and commercially available ionisation chambers with a DAP ratio (DAPR) between 20 cm and 10 cm as a quality index were tested. It turns that correction factors are needed if the transfer standard and the calorimeter have not the same sensitive surface and that the calibration coefficient of homemade secondary standards vary by about 1 % depending on the beam diameter up to 2 cm. The results are very encouraging and further studies are needed to check the behaviour of the DAP quantity in clinical situations where the radiation field is delimited by a multi-leaf collimator rather than a specially designed collimator. As the DAP quantity is not implemented in the treatment planning system, provided by the LINAC manufacturer, promising results have been found by converting the DAP into an evaluated point absorbed dose using 2D film dosimeters.

PTB studied the use of point like detectors to overcome the lack of primary standards for very small radiation fields [12]. The spatial response of commercially available ionisation chambers of different sizes (650 mm³ to 16 mm³) and shape (cylindrical and plane parallel) and diodes was studied in high energy photon and electron beams using a slit beam setup, 0.1 mm width, made of a lead blocks. The detectors were moved behind the slit and the spatial response was derived from the resulting signal. Monte-Carlo simulation confirmed these results but the lack of reproducibility from one chamber to another of the same type does not allow the provision of generic correction factors.

3.3 *To improve the consistency and traceability of proton and carbon ion beams, in particular novel types such as scanned particle beams.*

For hadron therapy, a new smaller water calorimeter was built for absorbed dose measurements in a 190 MeV proton beam and a 430 MeV/u carbon ion beam. The study of the chemical heat defect of water allows deriving correction factors. The recombination corrections for ion chambers under partial and time dependent irradiation conditions has been derived from Monte Carlo simulated dose distributions for proton beams. The fluence correction for materials such as plastic WT1, PW, PWDT, A150, polystyrene and polyethylene, and for detectors like alanine and radiochromic film has been evaluated. The energy dependence of alanine in scanned proton beams has been experimentally determined [2,3,4].

3.4 *To develop a metrological chain, from the primary standard to the end user's calibration and treatment verification, for the use of low energy x-rays for brachytherapy.*

New low energy micro x-rays generators are now available for improving the efficiency of low energy brachytherapy treatments and avoiding the use of radioactive isotopes. There currently is a lack of metrological chain from the primary standard in term of absorbed dose to water to the end user's calibration and treatment verification to give recommendations on a calibration chain for this new treatment modality. CMI and PTB worked to overcome this.

The first task, before establishing a primary standard in terms of absorbed dose to water, was to characterise the sources. Radiation fields produced by INTRABEAM and AXXENT were characterised by means of spectrometry (figure 7) and Monte Carlo calculation. To do that, correction of pile up for continuous spectra spectrometry was done successfully. Monte Carlo models of the micro x-ray generator produced by Carl Zeiss (the Intrabeam) and the Xofig Axxent tube were constructed by CMI. Both measurements and simulations were in good agreement.



Figure 7: PTB Ge spectrometer assembly

After characterising the source, the 3D dose distribution in water was investigated using X-ray storage foils and a plastic scintillator device developed at PTB. X-ray storage films have been characterised in terms of absorbed dose to water for energy range 8-50 keV, as well as radiochromic gel in terms of energy dependence and spatial resolution.

A primary standard in terms of absorbed dose to water based on an extrapolation chamber was built at PTB before this project. The determination of interaction coefficient for phantom material was done to finalise the reconstruction of this extrapolation chamber.

The INTRABEAM source is used with applicators for these High Dose Rate sources and the influence of the dose distribution of the two typical applicators used in clinics has been experimentally investigated. Finally, dose measurements were performed with standard uncertainty less than 3 %. [5,9]

3.5 *To develop a traceable measurement system for the verification of dose and distribution in complex radiation fields for the verification of treatment planning systems.*

Previous attempts to use a synthetic or natural based diamond detector as a secondary standard failed because of the lack of reproducibility. The PTW firm has made a new synthetic diamond detector, developed by ENEA and Tor Vergata Rome University, commercially available as a transfer dosimeter for photons and electrons in radiotherapy (figure 8). This detector is waterproof and does not need any biasing. The detector is based on a Schottky synthetic diamond photodiode. The nominal sensitive volume of the sensor is 0.004

mm³ which allows measurement in field sizes down to 1x1 cm². Its nominal response is about 1 nC/Gy. [1,8,10,14,15]



Figure 8: prototype of the Tor vergata/ENEA diamond based dosemeter

$K_{Q,Q0}$ values were measured for electron energies in the range 6 and 15 MeV and the range for photons down to 100 keV (Tables 1 and 2)

Real time *in vivo* dosimetry is one of the key issues of radiotherapy because it allows verifications during the treatment and therefore avoids errors. The Tor Vergata diamond detectors are optimised in a new configuration suitable for *in vivo* measurements.

Table 1: $K_{Q,Q0}$ values for high energy photons (6, 10 and 15 MV) in standard conditions.

TPR _{20,10}	$K_{Q,Q0}$	u %
0.657	0.987	0.004
0.731	0.994	0.003
0.755	0.990	0.004

Table 2: $K_{Q,Q0}$ values for high energy electrons in standard conditions.

E(Mev)	R ₅₀	$K_{Q,Q0}$	u %
6	2.65	0.993	0.003
9	4.03	1.000	0.004
10	4.15	1.001	0.004
12	5.23	0.999	0.004
15	6.52	1.004	0.004
18	7.97	1.005	0.004

In addition to the work on point detectors such as Alanine [6], the goal of the research programme was to characterise 2D (e.g. EBT3 gafchromic film, flexible storage phosphor plates and EPID) and 3D (gel) detectors [13] to be used for verification of complex dose distributions in photon and electron beams. The reading protocol for EBT3 gafchromic film has been optimised and the first results of STUK show that 1% accuracy in relative dose can be achieved. Spatial resolution and uncertainty of dose measurement with radiochromic film have been determined. Tests for depth dose and profile measurement showed a good agreement with point detectors.

One of the most promising dosimetry techniques is 3D dosimetry gel because it gives access in one measurement to the 3D distribution of the dose in a volume. UdA and LNE-LNHB studied Fricke gel. Fricke gels suffer from a diffusion of the species produced by the interaction of the radiations after irradiation. Therefore, the composition of a special Fricke gel has been optimised to ensure the required sensitivity and stability over time at least 5 hours after irradiation in collaboration with University Paul Sabatier (Toulouse France). This delay is enough to allow carrying the irradiated sample in front of the reading facility. It was

also necessary to optimise a special manufacturing protocol to ensure the reproducibility of the gel, it was done by producing a double concentrated gel in quite large volume to store it before using it to produce gels for experiments.

Two main methods are used to read a gel, MRI and optical reading. It was chosen here to use MRI because MRI facilities are usually located in the vicinity of radiotherapy services. A multi-echo reading protocol was adapted to the new Fricke gel MRI.

A first evaluation of the energy response exhibits a flat response in terms of absorbed dose to water for high energy photons between 1 MeV and 20 MV LINAC radiation quality and a variation of 20 % for low photons energies below 250 keV. The dose threshold was about 1 Gy which is enough to allow studying the dose to the organ at risk in the vicinity of the tumour but still not enough to look at the scattered radiation dose far from the tumour. The dose range goes up to 60 Gy.

Software for the automatic analysis of the MRI image to calculate 3D dose distribution from the raw reading has been developed. The goal is to launch a new dosimetry service operated by UdA within the next months. The components of the gel will be sent to the medical physicist at the hospital by UdA to manufacture the gel and fill in a phantom, then the medical physicist will irradiate an anthropomorphic or semi anatomical phantom as for a real treatment and read the gel using the multi-echo protocol given with the gel at hospital, finally the raw results in DICOM format will be sent to the remote calculation centre at UdA which will send back the 3D dose distribution to the treatment centres. All the steps for launching this service are ready and the service will be launched within a few months.

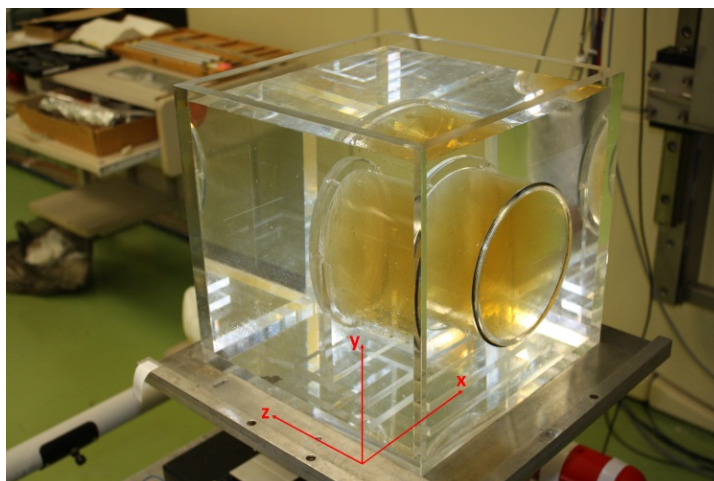


Figure 9: View of gel cylinder irradiated in a 30x30x30 cm³ water phantom in front of a 6 MV LINAC photon beam.

EPID lies between 2D and 3D techniques because the measurement itself gives 2D information but multiple angle acquisitions and mathematical reconstruction allow the building of 3D models of the dose distributions inside the patient. As the measurement is made during the treatment, the result is a “true” dose distribution, measured in vivo, which can be used to validate the TPS calculations. NPL did the first step toward this goal that is to say to study the characteristics of the detector EPID. Angular and energy responses have been measured and validated against Monte Carlo calculation, with some dependency on the (imprecisely known) detector material composition.

Using the detectors mentioned above, the aim is to develop, validate, compare and characterise (in terms of uncertainty budget) measurement methods for the 2D/3D verification of the treatment planning system. These methods can be based on one dosimeter or the association of several point, 2D, and 3D dosimeters. The validation is done in an anthropomorphic or semi anatomical phantom (to be as close as possible to the clinical conditions) on the basis of the comparison of the results of the measurement methods and TPS calculations. An anatomical female torso water phantom (figure 10) and 2 semi-anatomical phantoms – one for mastectomy and another for “head and neck” (figure 11) – were built by STUK and a special phantom with different tumour sizes for testing the ME40 organic plastic scintillator system built by DTU (figure 12).



Figure 10: Anatomical female torso water phantom in which different type of chamber and heterogeneities can be set.



Figure 11: Anatomical head and neck water phantom with polyethylene wall 1 mm thick in which PTW semiflex chamber can be inserted in fixed position.

These phantoms correspond to suitable cases for investigation to be chosen among those for which the TPS calculations and the measurements have well known difficulties i.e. where high gradient doses are encountered, such as in dynamic rotational treatment modalities, and in the presence of heterogeneities and organ at risk in the vicinity of the tumour. Such phantoms are intended to be scanned for further TPS calculations and detectors are positioned within it during the simulated treatment for real time or delayed measurements of doses. A pilot study of the external quality control for IMRT (Intensity Modulated Radio Therapy) has been made with alanine put in the CIRS thorax phantom (figure 7). This study exhibits a difference of 1.6 % between alanine at TPS doses while the standard uncertainty on alanine dosimeter was 1.5 %. For organic scintillator in the especially designed DTU phantom the reported deviations were of about 1 % while the standard uncertainty on the scintillator measurement was of about 1 %. A series of recommendations or guidelines will be written and disseminated to the European radiotherapy community.



Figure 12: CIRS (left) and DTU phantoms.

3.6 Summary of the key results

- New reference in terms of absorbed dose to water at 2 cm depth based on a mixed water/graphite calorimeter, advances in the same reference based on an extrapolation chamber
- First direct comparison in the world in terms of absorbed dose to water at 2 cm depth with selected radiation qualities representative of the medium energy X ray used for radiotherapy
- Validation of the first large area graphite calorimeter in the world for DAP measurement made to overcome the lack of traceability of absorbed dose at a point in small radiotherapy beams
- Important new knowledge to improve the consistency and traceability of proton therapy references especially for scanned proton beams
- First traceability chain established in the world for low energy photon produced by mini X ray generators
- First synthetic diamond dosimeter commercially available in the world by project collaborator PTW
- New 3D fricke gel dosimeter with MRI reading for an end-to-end TPS verification based on the comparison of the calculated and measured dose distributions
- Enhancement of the knowledge of characteristics of dosimeters used for insertion into specially designed phantoms for end-to-end absorbed dose to the tumor verifications
- Pilot study of external quality control for IMRT using a CIRS thorax phantom

4 Actual and potential impact

Dissemination of results

The project outputs have been shared widely with the metrology, instrumentation and clinical communities. 19 papers were published in peer reviewed journals or as book chapters and 58 oral or poster presentations were given at conferences.

Early Impact

The project developed methodologies, primary standards and guidance for new complex radiation treatments. The following achievements show how the results from the project are being used in research projects and in instrument development:

- The diamond detector developed by ENEA and Tor Vergata University within the framework of this contract is now included in a PTW commercially available dosimeter. This detector allows a better evaluation of output factors when commissioning the medical LINAC, so subsequently a better accuracy of the dose distribution of the treatment calculated by the treatment planning system.
- Reference standards in terms of DAP have been established to overcome the lack of direct traceability for small fields in high energy photons beams.
- Calibration with traceability to primary reference is now established for low energy x-rays in brachytherapy.
- The 3D gel dosimetry is ready to be used by end users for checking the organ at risk doses through a comparison with the TPS calculations.
- Correction factor for scanned hadron beams have been established to make available absorbed dose to water references
- Metrological use of 2D Gafchromic film has been improved to reach 1% uncertainty opening the way to use them for in vivo dosimetry.

Potential impact

The results of the project will have significant effect of future technology for radiation treatment. The work has contributed to the research on radiation metrology, and reflects the continuous evolution of the modalities and complexities of treatments. Examples include:

- The feasibility of the DAP concept for primary standard as a replacement of the dose absorbed at a point for the small fields is proven, but further improvements are needed in terms of transfer dosimetry to reach an industrial stage.
- The new chain of traceability was established for the brachytherapy electronic units, which represents an essential advancement for the safety of treatments using this modality. Prior to this work, only an indirect traceability could be achieved.
- This diamond detection technology is well suited for in vivo dosimetry to replace silicon detectors which are not tissue equivalent.
- It is not possible to do a calibration in the same conditions as those of the treatment, therefore checking the treatment plans in conditions as similar as possible to the reality is also a remarkable result allowing testing of the plans of treatment, and detection of possible errors before they have consequences. So the phantom design and built within this work and the pilot study shows reassuring results. Based on gel dosimetry studied in this work a 3D dosimetry service could be proposed to end users in the future.
- The working group for updating the IAEA 398 protocol will take advantage of the results of the project.
- The use of EPID for in vivo dosimetry was checked and the dose characteristic if the EPID were studied showing that extra work are necessary since the geometrical and material characteristics must be know with more accuracy.
- The new anthropomorphic or semi anthropomorphic phantom are potential candidates for routine use, with further improvements.

5 Website address and contact details

Website: radiotherapy-emrp.eu

Coordinator email address: jean-marc.bordy@cea.fr

6 List of publications

1. Characterization of a synthetic single crystal diamond Schottky diode for radiotherapy electron beam dosimetry, C Di Venanzio, M Marinelli, E Milani, G Prestopino, C Verona, G Verona-Rinati, MD Falco, P Bagalà, R Santoni, M Pimpinella, Medical Physics February 2013, 40(2), 021712(9 pp) DOI:10.1118/1.4774360
2. Fluence correction factors for graphite calorimetry in a low-energy clinical proton beam: I. Analytical and Monte Carlo simulations H. Palmans, L. Al-Sulaiti, P. Andreo, D. Shipley, A. Lühr, N. Bassler, J. Martinkovic, J. Dobrovodský, S. Rossomme, R. A. S. Thomas and A. Kacperek, Physics in Medicine and Biology 30 Apr 2013, Phys. Med. Biol. 58(10), 3481-3499
3. Dosimetry auditing procedure with alanine dosimeters for light ion beam therapy: results of a pilot study A. Ableiter, S. Vatsnitsky, R. Herrmann, N. Bassler, H. Palmans, P. Sharpe, S. Ecker, N. Chaudhri, O. Jäkel, D. Georg, Radiotherapy and Oncology 22 Jul 2013, Radiother. Oncol. 108(1), 99-106
4. Conversion from dose-to-graphite to dose-to-water in an 80 MeV/A carbon ion beam S. Rossomme, H. Palmans, D. Shipley, R. Thomas, N. Lee, F. Romano, P. Cirrone, G. Cuttone, D. Bertrand and S. Vynckier, Physics in Medicine and Biology 23 Jul 2013, Phys. Med. Biol. 58(16), 5363-5380
5. Uncertainties associated with brachytherapy source calibrations and dose calculations DeWerd, Larry A.; Rivard, Mark J.; Selbach, Hans-Joachim, Book article Comprehensive brachytherapy : physical and clinical aspects ; (Imaging in medical diagnosis and therapy): (2013), 213 - 223
6. Difference in the relative response of the alanine dosimeter to megavoltage x-ray and electron beams Anton, Mathias; Kapsch, Ralf-Peter; Krauss, Achim; Voigts-Rhetz, Philip von; Zink, Klemens; McEwen, Malcolm Physics in Medicine and Biology: 58 (2013), 10, 3259 - 3282
7. Calorimetric determination of the absorbed dose to water for medium-energy X-rays with generating voltages from 70 kV to 280 kV Krauss, Achim; Büermann, Ludwig; Kramer, Hans-Michael; Selbach, Hans-Joachim, Physics in Medicine and Biology: 57 (2012), 19, 6245 – 6268
8. Radiotherapy electron beams collimated by small tubular applicators: characterization by silicon and diamond diodes P Bagalà, C Di Venanzio, M D Falco, A S Guerra, Marco Marinelli, E Milani, M Pimpinella, F Pompili, G Prestopino, R Santoni, A Tonnetti, C Verona, G Verona-Rinati Physics in Medicine and Biology: 58 (2013), 22, 8121-8133
9. Monte Carlo simulations of miniature brachytherapy X-ray tubes (in Czech) J. Šolc, L. Burianová, T. Schneider Bezpečnost jaderné energie. 2013, vol. 21, no. 11-12, pp. 347-351. ISSN: 1210-7085.
10. Dosimetric characterization of a synthetic single crystal diamond detector in a clinical 62 MeV ocular therapy proton beam Marco Marinelli, F. Pompili, G. Prestopino, C. Verona, G. Verona-Rinati, G.A.P. Cirrone, G. Cuttone, R.M. La Rosa, L. Raffaele, F. Romano, C. Tuvè, Nuclear Instruments and Methods in Physics Research Section A, 767 (2014) 310–317, 2014
11. Dosimetric characterization of a microDiamond detector in clinical scanned carbon ion beams M. Maronelli, G. Prestopino, C. Verona, G. Verona-Rinati, M. Ciocca, A. Mirandola, A. Mairani, L. Raffaele, G. Magro, Medical Physics, 42 (4), 2085-2093, 2015 DOI:10.1118/14915544

12. Measurement of spatial response functions of dosimetric detectors Steffen Ketelhut and Ralf-Peter Kapsch, *Physics in Medicine and Biology*: 60 (2015), 6177-6194
13. Energy dependence of Fricke-xylenol orange gel and gel based on Turnbull blue for low-energy photons J. Solc, V. Sochor and P. Kozubíková, *J. Phys.: Conf. Ser.* 573 012069 doi:10.1088/1742-6596/573/1/012069
14. A novel synthetic single crystal diamond device for in-vivo dosimetry Marco Marinelli, G. Prestopino, A. Tonnetti, C Verona, G. Verona-Rinati, M.D. Falco, P. Bagalà, M. Pimpinella, A.S. Guerra, V. De Coste, *Medical Physics*: 42 (2015), 8, 4636-4644 DOI:10.1118/1.4926556
15. Characterization of a microDiamond detector in high-dose-per-pulse electron beams for Intra Operative Radiation Therapy C. Di Venanzio, Marco Marinelli, A. Tonnetti, G. Verona-Rinati, M.D. Falco, M. Pimpinella, A. Ciccotelli, S. De Stefano, G. Felici, F. Marangoni, *Physica Medica* Volume 31, Issue 8, December 2015, Pages 897-902, DOI: <http://dx.doi.org/10.1016/j.ejmp.2015.06.008>
16. First International Comparison of Primary Absorbed Dose to Water Standards in the Medium Energy X-ray Range Ludwig Büermann, Antonio Stefano Guerra, Maria Pimpinella, Massimo Pinto, Jacco de Pooter, Leon de Prez, Bartel Jansen, Marc Denozziere and Benjamin Rapp, *Metrologia*, Volume 53, Technical Supplement
17. A graphite calorimeter for absolute measurements of absorbed dose to water: application in medium-energy x-ray filtered beams Massimo Pinto, Maria Pimpinella, Maurizio Quini, Marco D'Arienzo, Iordana Astefanoaei, Stefano Loreti, and Antonio Stefano Guerra, 2016 *Phys. Med. Biol.* 61 1738 doi:10.1088/0031-9155/61/4/1738
18. Accuracy of a dose-area product compared to an absorbed dose to water at a point in a 2 cm diameter field S. Dufreneix, A. Ostrowsky, B. Rapp, J. Daures and J. M. Bordy, *Medical Physics*, 2016, 43, 4085-4092, DOI:10.1118/1.4953207
19. Using a dose-area product for absolute measurements in small fields: a feasibility study Dufreneix, Stephane; Ostrowsky, Aime; Le Roy, Maïwenn; Sommier, Line; Gouriou, Jean; Delaunay, Frank; Rapp, Benjamin; Daures, Josiane; Bordy, Jean-Marc, 2016 *Phys. Med. Biol.* 61 650 doi:10.1088/0031-9155/61/2/650