

TOWARD A MULTI-MODALITY APPROACH TO RADIOTHERAPY FOR CANCER TREATMENT IN UK

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In the UK cancer is the leading cause of mortality in people under the age of 75 and accounts for one in four deaths overall. Cancer is currently the third largest NHS (National Health Service) disease programme. Radiotherapy is one of the main forms of cancer treatment, with an overall cure rate of 40 %. In this paper we review the different types of radiotherapy treatments used and we summarise their current status. Particular emphasis will be placed on a new approach to radiotherapy: the **multi-modality** approach. We will explain how to develop this **multi-modality** approach and what will be the benefits to the patients. We will discuss the technological challenges faced in the development of such a **multi-modality** approach to radiotherapy and the advances needed in the fields of dosimetry and quantitative imaging. We will present two examples of R&D projects for future technologies: in-vivo dosimetry and TOF PET imaging.

1. Introduction

Each year in the UK 293 000 people are diagnosed with cancer and 155 000 people die from cancer. This makes cancer the leading cause of mortality in people under the age of 75 and accounts for one in four deaths in the UK overall. The incidence of cancer is also rising due to population ageing, increasing obesity levels and changes in lifestyle that are making some types of cancer more common. For these reasons the UK National Health Services (NHS) has made of cancer its third largest disease programme, following mental health and circulatory diseases [1].

Cancer is a disease of the cells. Normally, cells divide in an orderly and controlled manner. When, for some reasons not so well understood, cells stop responding to normal cellular control mechanisms, they start to accumulate abnormally, creating a growth or lump called tumour. A benign tumour is a local growth, with infiltration of small groups of cells in adjacent tissues and no spread to other parts of the body. If the benign tumour continues to grow, it may cause problems by pressing on surrounding organs. A malignant tumour, also called cancer, is a more aggressive type of tumour, with the ability to spread beyond the original area. If a malignant tumour is not treated, cells may break away from it and spread distantly to other parts of the body, via the bloodstream or the lymphatic system, creating new tumours, called metastasis. When the cancer cells reach a new part of the body, they may form a new tumour, called secondary cancer or metastasis. There are more than 200 different types of cancer.

Radiotherapy in the UK is a major form of cancer treatment. Radiotherapy is indeed given to one third of all the cancer patients, which corresponds to 10 - 15 % of the overall UK population. The overall cure rate achieved with radiotherapy is 40 % [2]. For some types of cancer, like breast cancer and stage 1 larynx cancer, the cure rate can be as high as 90 - 95 %. Radiotherapy is often not used in isolation by combined with other forms of treatment, namely surgery, chemotherapy and hormone treatments. Radiotherapy is administered in different ways that can be grouped in three main classes: 1) external beam radiotherapy; 2) internal radiotherapy and 3) binary radiotherapy.

A new **multi-modality** approach to radiotherapy is needed, in order to maximise its efficacy and benefits to the patient. The **multi-modality** approach is obtained by either selecting the most appropriate form of radiotherapy treatment depending from the tumour type or by combining various forms of radiotherapy when appropriate.

When treating a patient with radiotherapy, we need to ensure that that the right amount of radiation is delivered to the right place (the tumour). There is therefore a pressing need for developing new advanced technologies in the fields of dosimetry and quantitative imaging. New dosimetry systems will have to provide improved measurement of the dose delivered directly at the tumour site. New imaging systems will have to provide better quality, more accurate and faster imaging to identify and locate more precisely the tumour inside the body of the patient.

In this paper we review the different forms of radiotherapy treatment and summarise their current status in the UK. We examine in detail the **multi-modality** approach and give examples of application to specific clinical cases. We review the current-state-of-the-art in the fields of dosimetry and quantitative imaging. And we identify and discuss the advances needed to meet the technological requirements for the development of this **multi-modality** approach.

2. Radiotherapy treatments

It is well known that radiation damages the DNA of cells [3]. For radiation such as photons, electrons and protons, the dominant mechanism is indirect ionisation: the radiation ionises water, creating free-radicals, which then damage the atoms in the DNA chain. High-LET particles, such as carbon and other light ions, instead tend to damage the DNA by directly ionising the atoms in the DNA chain. The DNA damage created in the cells is passed on to new cells when they are formed (cell division). The DNA damage is therefore accumulated in the cells, causing them to reproduce more slowly and eventually to die. All cells have mechanisms for repairing DNA damage, although cancer cells have a diminished ability to repair this damage compared to normal, healthy cells. The response to radiation varies from tissue

to tissue. For example lung cancer tissue is highly radiation-resistant, while lung healthy tissue is on the contrary highly radiation-sensitive. Another parameter that influences the radiation-sensitivity of a cancer is its level of oxygen. When irradiated, oxygen forms free-radicals that then damage the DNA, increasing the effectiveness of a given dose. Low level of oxygen (hypoxia) can therefore increase the resistance to radiation. During their growths, cancers can restrict their blood supply, becoming hypoxic. Hypoxic cancer may be up to two, three times more radiation resistant than cancer with a normal level of oxygen [4].

The total amount of radiation, dose, prescribed to the patient depends on the type and stage of cancer being treated. And it can vary from tens of Gy to 100-120Gy.

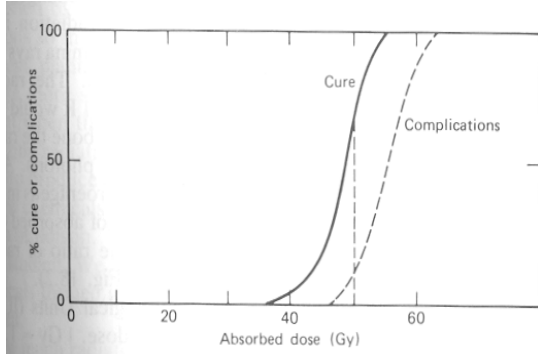


Fig. 1. The probabilities of curing the cancer (killing the cancerous cells) and creating complications (damaging the healthy cells) as function of the absorbed dose. For this case a total dose of 50Gy will have around 60 % probability of curing the cancer and an associated 10 % probability of creating complications.

The key to a successful radiotherapy treatment is therefore to find the optimal dose that maximises the probability of curing the cancer and at the same time keeps the complications to an as low as possible level. Otherwise stated, the key to a successful radiotherapy treatment is to find ways of separating as much as possible the two curves, moving the one for cure toward the left of the plot (lower doses) and the one for complication toward the right of the plot (higher doses). One way of increasing the separation between the two curves is by administering the total dose prescribed in several consecutive shots, called fractions. A typical fractionation schedule is about 2Gy per day, five days a week, over several weeks. The main reason for fractionation is as follow. If the same total amount of dose is given in several fractions instead of one fraction only, the cells will have time to repair themselves between fractions. Given that cancerous cells are less efficient in repairing themselves than normal cells, a fractionated treatment will reduce the amount of damage to the healthy cells, while maintaining a high level of damage to the cancerous cells.

There are various forms of radiotherapy treatments, which can be classified in three big groups: 1) external beam radiotherapy (described in 2.1.); 2) internal radiotherapy (described in 2.2.) and 3) binary radiotherapy (described in 2.3.).

2.1. External beam radiotherapy

In external beam radiotherapy the source of radiation is external to the body of the patient. A radiation beam is created by an accelerator outside the body of the patient body and is then focused on the tumour inside the body. Three are the types of beam used in external beam radiotherapy: X-rays, electrons and charged particles (proton or light ions).

X-ray radiotherapy uses a MV beam of X-rays. The X-ray beam is produced by the bremsstrahlung of an electron beam from a LINAC on a primary target. The distribution of the dose delivered to the tumour has evolved throughout the years: at the beginning the dose distribution was simply a rectangular prism (conventional radiotherapy) that was covering not only the tumour but also surrounding healthy organs; the introduction of shielding blocks allowed shaping the rectangular prism to a more complicated form that covered the tumour while avoiding as much as possible the surrounding healthy tissues (conformal radiotherapy). The latest development is Intensity Modulated Radio Therapy (IMRT). IMRT uses a complicated multi-leaf collimator that allows changing the intensity of the beam during treatment. With IMRT complicated concave dose distributions can be created, which are extremely important for treating tumours wrapped around vital organs like the spinal cord for example. X-ray radiotherapy is the form of radiotherapy treatment most widely used in the UK and is used for almost all types of cancer, with the only exception of stomach and ovarian cancer and carcinoid tumours.

Electron radiotherapy uses an electron beam of energy in the range 4 - 22 MeV. The electron beam is created by the same machine used for X-ray radiotherapy, where the primary target has been removed and the current has been lowered. Several are the disadvantages of electron radiotherapy. The beam contains a large contamination of low energy γ , created by the interaction of the beam with machine elements; along the path between the exit of the LINAC and the patient, the beam suffers a high degree of scatter in air that degrades its characteristics. An electron beam is very

difficult to steer: for this reason there is no equivalent of IMRT for electron radiotherapy. The calculation of the dose distribution for treatment planning is very difficult and can only be done with time-consuming simulations. For all these reasons electron radiotherapy is no longer of common use and is limited to superficial tumours, located at a maximum depth of few cm from the skin.

Charged particle radiotherapy uses beams of either protons or light ions (carbon or helium for example) generated by an accelerator. This form of external beam radiotherapy takes advantage of the more localised energy deposition of protons and light ions in respect to X-rays and electrons. Protons and light ions deposit the majority of their energy at the end of their range (Bragg peak). By tuning the energy of the beam it is possible to choose the range so that the beam stops at the depth where the tumour is located. No dose is therefore deposited behind the tumour. The main areas of application for charged particle radiotherapy are for paediatric tumours and for tumours located adjacent to vital organs. In the UK there is currently only one proton centre at the Clatterbridge Hospital: the value of the proton beam energy (70MeV) limits its application to eye tumours only.

2.2. Internal radiotherapy

In internal radiotherapy the source of radiation is placed inside the body of the patient near or inside the tumour. Two are the types of internal radiotherapy: brachytherapy and radiopharmaceutical therapy, also called radioisotope therapy.

Brachytherapy uses sealed sources, which are implanted in the body of the patient next to or inside the tumour. Nowadays the most common form of treatment is temporary brachytherapy, where the source is left in the body for a limited amount of time, usually minutes or hours, before being withdrawn. In the less common permanent brachytherapy, after implantation the source is left permanently in the body of the patient. The half-lives and the activities of the sources used are such that the levels of radiation emitted fall to almost zero after few months. In the case of permanent implantation, the sources will therefore become inactive eventually. The most common sources used are ^{137}Cs , ^{192}Ir , ^{60}Co , ^{125}I and ^{198}Au , shaped in various ways: wires, balls and seeds. The main advantage of brachytherapy is that the mean free-path of the irradiation is very short. The dose deposition is therefore highly localized around the source and exposure to radiation of further away OAR is reduced. This means however that brachytherapy can only be used to treat small, localised cancer. Another advantage of brachytherapy is that, given that the source is placed inside the body, the irradiation of the tumour is not affected by the patient movement. Brachytherapy is used to treat a large number of cancer types, although the four most common are cervix, breast, prostate and skin cancer.

In radiopharmaceutical treatments, a radioactive liquid is given to the patient either to drink or by injection. The radioisotopes of most common in the UK use are ^{131}I , ^{32}P and ^{89}Sr . The key to a successful treatment is the use of radiopharmaceuticals that effectively bind with the tumour, while clearing very fast from the rest of the body. Much effort is currently put in the research of new molecules (antibodies, peptides and hormones) that satisfy these two requirements and are therefore good candidates for new radiopharmaceuticals. Another thriving research area is the development of new fast ways of radio-labeling the molecules, very important in case the radio-labeling is done using short lived isotope. In the UK, radiopharmaceutical treatments are used for thyroid cancer, blood disorders and secondary bone cancer. Iodine is metabolised by the thyroid and thyroid cells everywhere in the body: ^{131}I is therefore used to treat cancer in the thyroid and thyroid cancer metastases. Phosphorous is metabolised by the bone marrow: ^{32}P is therefore used to treat blood disorders as it gets absorbed in the bone marrow and stops excessive cell production. The metabolism of strontium is similar to that of calcium; for this reason strontium is accumulated in newly formed bones: ^{89}Sr is therefore used to treat secondary bone cancer (metastasis).

2.3. Binary radiotherapy

Binary radiotherapy combines an external beam of particles with a component given to the patient, enhancing in this way their effect. Two are the forms of binary radiotherapy: Boron Neutron Capture Therapy and Photon Capture Therapy.

Boron Neutron Capture Therapy (BNCT) combines the use of a beam of epithermal neutrons with ^{10}B injected in the patient. The epithermal neutron combines with ^{10}B to give ^{11}B , which after decays producing one α -particle and one ^7Li of high energy. The α -particle and ^7Li travel a very short distance, less than a cell diameter (12 μm), before depositing their energy.

Photon Capture Therapy (PCT) combines the use of an X-ray beam (the same beam used in external beam radiotherapy, see 2.1.) with a high-Z element given to the patient. In the interaction of the X-ray beam with the high-Z element, electrons are created via the photoelectric effect. Given that the photoelectric cross-section is proportional to Z^4 , the research is toward the identification of high-Z elements that can easily be concentrated in the tumour. As well as in BNCT, the electron range is quite short and the energy deposition is highly localised.

Binary radiotherapy (both BNCT and PCT) is still an experimental technique, at its early stage of development. The number of patients treated with this radiotherapy is less than 1000 worldwide. Binary radiotherapy is most suited for locally spread diseases with a high degree of infiltration in the surrounding tissues. The primary application so far, with encouraging preliminary results, has been the glioblastoma multiforme. This is the most highly malignant and

therapeutically persistent of all brain tumours. Epithelial neutrons are absorbed near to the skin. The energy and penetration depth of the X-ray beam are also limited (the photoelectric cross-section decreases with the third power of the beam energy, E^3). Binary radiotherapy can therefore be used only for superficial tumours, located on the skin or at a maximum depth of 3 - 4 cm from the skin.

3. The multi-modality approach to radiotherapy

The goal of radiotherapy is twofold: to cure the cancer and to protect the surrounding healthy tissues, guaranteeing in this way a high quality of life during and after treatment. In order to increase the efficacy of curing the cancer, the dose delivered to the tumour has to be increased (dose escalation). In order to protect the surrounding healthy tissues, the dose delivered to these tissues has to be minimised (reduced toxicity).

The goal of dose escalation and reduced toxicity is best achieved using all different forms of radiotherapy in a flexible way. It is indeed a well known fact that different treatment strategies are required depending on the type of cancer, on its stage and degree of spread. Unfortunately at present in the UK the different forms of radiotherapy treatments are not linked one to another. Treatments are usually carried out at the patient's local hospital. And not all hospitals offer the full range of treatments. IMRT for example is offered by only eight centres in UK. The main consequence of this current situation is that the efficacy of radiotherapy is far from optimal.

A new, unified approach to radiotherapy in the UK is required, in order to maximise the efficacy of radiotherapy and to achieve the goal of cure of cancer and high quality of life. This new approach will bring together the various forms (modalities) of radiotherapy treatments. We have therefore decided to name it the **multi-modality** approach to radiotherapy. This **multi-modality** approach will achieve improved cancer care. It will also achieve better local control of the disease and reduced toxicity and will therefore prove to be highly beneficial to the patients. The **multi-modality** approach to radiotherapy will be achieved in the two following, complementary ways, which will be chosen based on the analysis of each single clinical case:

1. Selection of the best treatment depending on the tumour type.
2. Combination of different treatments when appropriate.

The first treatment strategy option is using only one form of radiotherapy. The first selection criteria will be the tumour type. The different forms of radiotherapy are indeed targeted to different types of disease. All different types of external beam and internal radiotherapy are better suited for localised diseases; while binary radiotherapy is better suited for locally spread diseases with high degree of infiltration. The selection of the best form of treatment will need to take into consideration many other factors, like tumour size, the location of OAR and their position in respect to the tumour, the patient history, etc.

The second treatment strategy option is combining different forms of radiotherapy into a single treatment. How many and what types of radiotherapy to combine will be decided on a case-by-case basis and taking into account the same considerations as before. An example of this second treatment strategy is combining external beam radiotherapy with brachytherapy.

4. The technological challenge

It is mandatory to make sure that the right amount of radiation (dose) is delivered to the right place, e.g. the tumour. If the dose delivered to the tumour is too low, the treatment is ineffective; if the dose delivered to the tumour is too high we increase the toxicity and the risk of side effects and complications. If the dose is delivered at the wrong position (healthy tissue instead of tumour) we do not treat the tumour and increase the toxicity in the healthy tissues. Excellent dosimetry and imaging systems are therefore required for radiotherapy.

Making sure that the right dose is delivered to the right place in the **multi-modality** approach to radiotherapy presents new exciting technological challenges. Each form of radiotherapy has its own imaging and dosimetry requirements. The combination of radiotherapy treatments requires also the development of new treatment planning that can sum together the effects of each single treatment. New better dosimetry and imaging technologies are therefore required. These new technologies should be developed for a wide range of applications, so that they could be used with the different forms of radiotherapy treatments. They should also incorporate the possibility of combining the effects of the different radiotherapy treatments used.

In the UK big emphasis is currently placed on early diagnosis. The earlier the tumour is diagnosed, the higher is the probability of success in curing it. Detecting tumours in their early stage means however being able to image smaller volumes. This once again requires better imaging systems than the current ones.

It is clear that the **multi-modality** approach to radiotherapy and earlier diagnosis can only be achieved if new advanced technologies for dosimetry and imaging are developed. In 4.1. we review the state-of-the-art of the dosimetry and imaging technologies used in hospitals. In 4.2. we list the requirements for new technologies and present two R&D project examples of advanced technologies, one in the field of dosimetry and the other in the field of imaging.

4.1. The state-of-the-art

The dosimeters that are currently used in hospitals for radiotherapy are Thermo Luminescent Dosimeters (TLDs), diodes and MOSFET transistors. All these dosimeters are external: they are placed on the patient skin. They therefore measure the dose delivered to the skin and not to the tumour inside the body. TLDs do not provide real-time

information: the complex read-out procedure takes place usually sometime after the treatment fraction. Diodes and MOSFET dosimeters are wired, which makes them extremely cumbersome to use. They are also prone to non-linearity and large errors. For all these reasons the measurement of the dose delivered during treatment is not routine.

The calculation of the dose distribution to be delivered (treatment planning) heavily relies on imaging systems for the definition of the volume to be treated. It is worth noting that most imaging systems installed in hospitals (nuclear medicine, radiology, radiotherapy) use technologies developed initially for particle physics: scintillating materials and photon detectors. A state-of-the-art technique in nuclear imaging is Positron Emission Tomography (PET), routinely used for the disease diagnosis and staging. The operating principle of any PET system is the generation of two back-to-back 511 keV photons from the positronium decay. ^{18}F -fluorodeoxyglucose (^{18}F -FDG) is injected into the patient and is up-taken mainly by the tumour. The e^+ emitted by ^{18}F combines with the electrons in the patient's body to form positronium, which then decays in two back-to-back 511 keV photons. The two photons are detected by the PET scanner, a ring of scintillating crystals read out by photon detectors, which surrounds the patient. Two photons are considered coming from the same positronium if they are detected within a specified short "coincidence" time window. The position of the two scintillating crystals of the scanner in which the photons have interacted determines a straight line-of-response. The positronium decay point lies somewhere on this line-of-response. Image reconstruction algorithms are then used to determine the exact position of the annihilation point along this line. In the most widely used, conventional PET scanners, the exact position of the decay is calculated probabilistically from many millions of decay events.

4.2. The future

In order to provide better dosimetry, the new systems to be developed will need to overcome the limitations of the current dosimeters in use. First of all the new dosimetry system will have to measure the dose delivered to the tumour site and not to the skin. The measurement must be carried out in real-time, during or immediately after each treatment fraction. The dosimeter should also be designed so to provide measurement of the total dose delivered to the tumour when combining different radiotherapy treatments and ultimately to include the dose delivered during imaging procedures. Finally the system to be developed should be easy to use. Implantable in-vivo dosimetry is the ultimate solution for meeting all these requirements. In a project we are working on, the implantable in-vivo dosimetry system will consist of a dosimeter unit and of a wireless RFID communication system. The dosimeter unit will be permanently implanted in the body of the patient next to the tumour. This will ensure measurement of the dose at the right location. Being placed next to the tumour, the dosimeter will also register the dose every time the tumour receives radiation. This will provide measurement of the total dose accumulated in the tumour. The dosimeter unit will have on board the dose sensor, the read-out electronics and the transmitter of the RFID system. To use as dose sensors we have chosen MOSFET transistors with a calibrated sensitivity to radiation, called RadFETs. The RadFET signal is derived from the trapping of holes created by ionising radiation within the gate oxide. RadFETs have been used in particle physics experiments around the world, in real-time online radiation monitoring systems [5, 6]. A main advantage of the RadFET is its exceptionally small size. The RadFET is therefore one of the few devices that can be implanted deep in tissue and transmit dose information. The RFID system will be made of two parts: the transmitter on board the dosimeter unit and an external receiver. The receiver will be external to the patient and placed in the treatment room. The RFID communication system will transmit data from inside the body of the patient to the outside in real-time.

There is a pressing need for developing imaging systems that provide better quality, more accurate and quantitative imaging with a higher level of repeatability. Improved image quality both in terms of spatial and contrast resolution would also increase the accuracy in diagnosis and allow imaging smaller volumes of crucial importance for early diagnosis. Of paramount importance for improved imaging systems will be to have higher spatial resolution. Image quality will also be improved by increasing the linearity of the system and reducing its noise and drift. Another very important requirement for advanced imaging systems is to provide faster imaging. Faster imaging would reduce the radiation an average person gets when undergoing any medical imaging procedure. The number of times imaging procedures are performed could therefore be safely increased. And a new image could be taken at the beginning of each treatment fraction. In this way it would be possible to correct for any error that could have been made while setting-up the patient at the beginning of the treatment fraction. It would also allow detecting and taking into account any change in the tumour volume that could have occurred over the several weeks of treatment. Faster imaging would also open up the possibility of taking multiple images, with low additional doses to non-cancer tissues, during each treatment fraction. Tumours in moving organs, like the lung, could therefore be treated much more effectively. In the field of imaging we decided to concentrate on only one R&D project: the development of one new advanced PET scanner that uses the Time-Of-Flight (TOF) technique. In TOF PET [7], the difference in time of arrival of the two photons at the detecting elements (called simply detectors in the following) of the scanner is measured. The timing information is used to calculate the location of the positronium decay event on the line-of-response. If the decay point lies midway between the two detectors, the two photons arrive at the detectors at the same time; the further away from the middle the decay point is, the greater is the difference in time of arrival. A TOF PET scanner can therefore determine the position of the decay site with much greater accuracy and provide much better and faster imaging due to reduced dependence on the reconstruction software. A comparison between the operating principles of conventional PET and TOF PET is shown in Fig. 2, together with a schematic diagram of a TOF PET scanner.

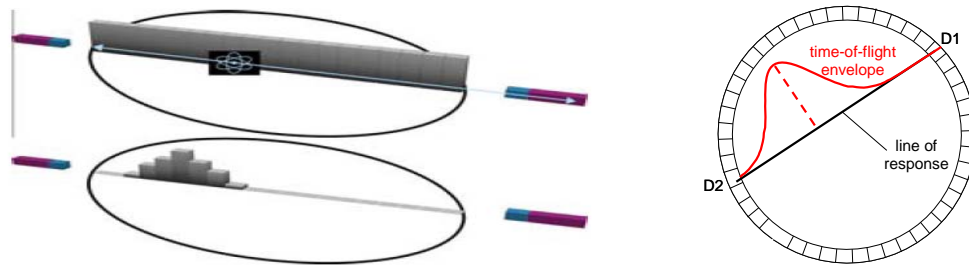


Fig. 2. On the left the principles of operation of a conventional PET and of a TOF PET scanner are compared. In a conventional PET scanner (above) each point on the line-of-response has the same probability of having been the decay point. In a TOF PET scanner the timing information allows the localisation of the decay point on the line-of-response. On the right is a schematic diagram of a ring of detectors: the two photons have interacted in detectors D1 and D2. In a conventional PET scanner the positions of D1 and D2 are used to determine the line-of-response shown. In a TOF PET scanner the timing information is used to locate the decay point with a certain precision, represented here by the time-of-flight envelope.

It is clear that the faster are the detectors, the narrower is the time-of-flight envelope and the better the decay event localisation will be. For TOF PET to be advantageous in respect to conventional PET, the scanner has to provide timing resolution of at least 100 ps and ideally below 30 ps. The key for the successful development of TOF PET is therefore to identify commercially available fast scintillating materials and photon detectors to be used in the scanner. We carried out a market investigation to identify the best candidate scintillating materials and photon detectors. We selected two scintillating materials: $\text{Lu}_{1.8}\text{Y}_{0.2}\text{SiO}_5(\text{Ce})$ (in short LYSO) and $\text{LaBr}_3(\text{Ce})$. Both materials are produced by Saint-Gobain Cristaux et Detecteurs with trade names PreLudeTM420 (LYSO) and BrillanCeTM380 ($\text{LaBr}_3(\text{Ce})$). For the read-out of the scintillating materials we selected a recently developed photon detector: the solid state Silicon PhotoMultiplier (SiPM). In Fig. 3, *a* is a picture of sample LYSO and $\text{LaBr}_3(\text{Ce})$ crystals, while in Fig. 3, *b* is a picture of a couple of SiPMs mounted on read-out boards.

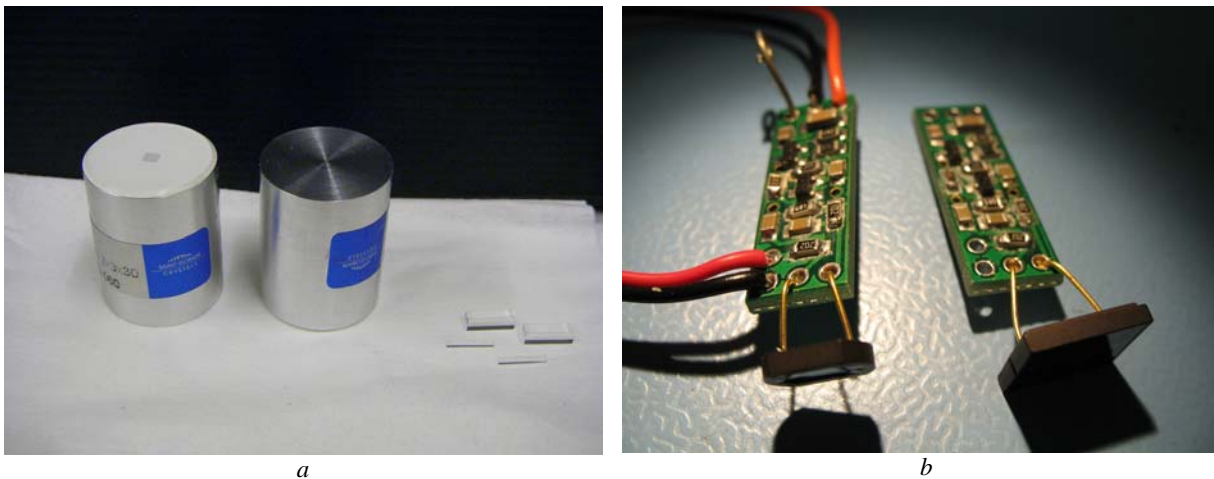


Fig. 3. *a* - on the left are two $\text{LaBr}_3(\text{Ce})$ crystals in their packaging placed inside an aluminium housing ($\text{LaBr}_3(\text{Ce})$ is a highly hygroscopic material), while on the right are four LYSO crystals; *b* - two SiPMs mounted on read-out boards.

The SiPM has a fast response time, making it an ideal candidate for use in a PET scanner, but has not been used in commercial systems to date. Another very interesting characteristics of the SiPM is that it can work reliably in high intensity magnetic fields. This feature of the SiPM may enable the development of a combined PET and MRI (Magnetic Resonance Imaging) scanner, to provide an even more powerful and versatile multi-modality imaging system. We performed an initial characterisation of SiPMs bought from three different manufacturers (Hamamatsu, Photonique and SensL) and measured the timing resolutions offered by single SiPMs and by pairs of identical SiPMs. The best timing resolution measured were 20 ps for the single SiPM and 40 ps for SiPM pairs [8]. We built and tested various two-channel demonstrator systems. The timing resolutions offered by the various two-channel demonstrator systems were measured using two different β^+ emitter, ^{22}Na and ^{18}F . The best timing resolutions measured were 430 ps with LYSO crystals and 790 ps with $\text{LaBr}_3(\text{Ce})$ crystals [8]. In Fig. 4 is a pictures of a two-channel demonstrator system, together with the data acquisition system based on a fast digital oscilloscope.

These preliminary results are extremely encouraging and show the potentials for a substantial improvement in respect to the current generation of clinical TOF PET scanners. We are planning further investigations, including the construction and testing of a dual-head demonstrator system. This demonstrator system will be composed of two diametrically opposed identical heads. Each heads will have a planar (2D) array of channels.

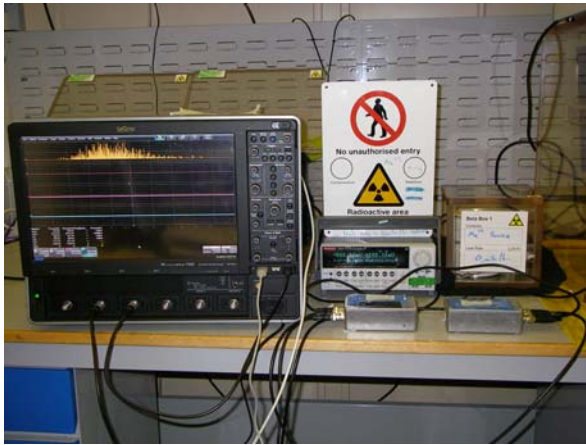


Fig. 4. One of the two-channel demonstrator systems built, together with the fast digital oscilloscope used for the read-out of the demonstrators.

approach would therefore be highly beneficial to the patient, being more effective in treating cancer while guaranteeing a good quality of life during and after treatment.

The technological advances needed for the implementation of the **multi-modality** approach were discussed. It was demonstrated that the two crucial areas of research are dosimetry and quantitative imaging. A list of requirements for the new technologies was compiled, based on an analysis of the state-of-the-art. Two examples of R&D projects for future technologies were given: in-vivo dosimetry for improved dosimetry and TOF-PET for improved imaging.

The efficacy of radiotherapy, one of the main cancer treatments, can and should be improved adopting the **multi-modality** approach described in this paper. Advanced technology holds the key to the implementation of **multi-modality**. The time to adopt the **multi-modality** approach and to work on new technologies for improved cancer care is now.

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5. Conclusions

Cancer, a cell disease, is the leading cause of mortality in people under the age of 75 in the UK, where it accounts for one in four deaths overall. And its incidence is rising due to population ageing, increasing obesity levels and lifestyle changes. Recently, the UK National Health Services (NHS) has made of cancer its third largest disease programme.

In the UK, radiotherapy is a major form of cancer treatment, being given to one third of all the cancer patients and with an overall cure rate of 40%. The various types of radiotherapy treatment were reviewed, together with their status of use in the UK.

The new **multi-modality** approach to radiotherapy was presented. It was shown how this approach would increase the efficacy of radiotherapy in curing cancer by escalating the dose delivered to the tumour, whilst minimising side effects and complications by reducing the toxicity in the healthy tissues. The **multi-modality**