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Review

## Radiotherapy quality insurance by individualized in vivo dosimetry: State of the art

*Dosimétrie individuelle in vivo pour le contrôle de qualité en radiothérapie : état de l'art*

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### Abstract

The quality insurance in radiotherapy in the frame of highly complex technical process as Intensity modulated radiotherapy (IMRT) needs independent control of the delivered dose to the patient. Actually, up to now, most of the radiotherapy treatments rely only on computed dosimetry through a rather complicated series of linked simulation tool. This dosimetry approach requires also qualified treatment means based on cautious quality insurance procedures. However, erroneous parameters could be difficult to detect and systematic errors could happen leading to radiotherapy accidents. In this context, in vivo dosimetry has a critical role of final control of the delivered dose. As many beam incidences and ports are used for any photontherapy treatment, external control could be very tedious and time consuming. Therefore, innovations are needed for in vivo dosimetry to provide ergonomic and efficient tools for these controls. This paper presents a review of technologies and products that can be used for in vivo dosimetry. It proposes also a reflection on the concepts to develop future devices suitable for this purpose. The technical means with their physical principles are reviewed, the clinical experiences demonstrating the feasibility of new techniques are then summarized and finally, the early clinical use and its impact on clinical practice is review.

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*Keywords:* In vivo dosimetry; Electronic dosimeter; Semiconductors; Radiotherapy; Implantable radiation detectors

### Résumé

La complexité croissante des techniques de radiothérapie externe, telles que la radiothérapie de conformation avec modulation d'intensité (RCMI), nécessite des contrôles de qualité reposant autant que possible sur des informations dosimétriques obtenues in vivo indépendantes du calcul de la dose. En effet, à ce jour, la plupart des informations dosimétriques sont obtenues par la modélisation de la distribution de la dose sans aucune mesure propre à chaque patient traité. Aussi, la fiabilité de cette modélisation repose-t-elle sur une cascade de systèmes dont le contrôle de qualité doit assurer la validité de chaque étape. Cependant, le nombre de paramètres des irradiations modernes devient très important, plusieurs centaines par traitement et leur vérification a priori pourrait être fragile dans certaines circonstances. Dans ce contexte, la disponibilité d'un moyen de mesure direct de la dose absorbée dans le volume cible du traitement, pour un patient donné, permettrait une sécurité renforcée pour les traitements les plus complexes. Cependant, les moyens techniques disponibles à ce jour ne sont guère pratiques et nécessitent une mise en œuvre longue et compliquée, impropre à la pratique routinière. Cette revue fait le point sur ces méthodes et leurs résultats cliniques et tente de définir les caractéristiques techniques idéales pour réaliser une dosimétrie in vivo, indépendante, en routine clinique.

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*Mots clés :* Dosimétrie ; Dosimètre électronique ; Semi-conducteur ; Radiothérapie ; Détecteur implantable

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## 1. Introduction

The use of high precision technology in radiotherapy for the treatment of cancers, such as 3D conformal radiotherapy and IMRT results in the need of developing new Quality assurance systems (QA) for individualized check of every treatment. These highly sophisticated treatments need a large number of human/machine interfaces that could result in erroneous information among hundreds of parameters. This type of human error is typically difficult to find and could easily result in systematic alteration of the fraction dose occurring along the whole treatment, typically including 25 to 40 sessions, resulting in very large under- or overexposure. The consequences for the patient are potentially life threatening, respectively due to a lack of cure and relapse of the cancer, or a complication with abnormal destruction of healthy tissues. Therefore, a risk of serious accidents is to be feared. Actually, a series of accidents has happened in France demonstrating the reality of this risk. For example, mistransmission of wedge filter command or misunderstanding of such command in new computer system have occurred recognized accidents in two radiotherapy centers these recent years with some death among the ill-treated patients [1,2]. However, more classical accidents could also happen with direct manual mismanipulation usually not very dangerous as being generally not systematical along a whole treatment, except in one-session treatment as radiosurgery where dramatic consequences could be observed as recently reported [3].

Beside these human errors that are efficiently avoided by recording and verification procedures [9], it could be also observed some random errors appearing at anytime during the treatment, able to alter the total dose that will be delivered. For example, the erroneous stop of a beam due to random misregistration of the session dose by the software itself has been observed in our department. This type of error needs a continuous survey of any treatment and not only the assessment of the first session of each phase of the treatment.

To avoid dramatic consequences for the patient, a set of quality controls should be carried out during the planning, the initiation and the course of the treatment. Comprehensive literature on this topic could be found [25], however, most generally in radiotherapy, the absorbed dose in the target volume, that is the “final product” of the treatment, is not measured but only calculated through a modelization of the treatment by the Treatment planning system (TPS) software. The only way to state that the planning dose is accurately delivered to the target is to measure it in the target itself. However, this is not an absolute protection against alterations that would deliver abnormal doses outside of the target. Therefore, it could be proposed to develop the use of in vivo implanted dosimetry either for the targeted volume or for sensitive organs in the vicinity of the target volume.

A common use of in vivo dosimetry is the control of total body irradiation that requires detectors at the entrance port and the exit port of the irradiation. This is a tedious procedure that theoretically would require a number of detectors equal to twice the number of beams for its application to regular external radiotherapy. Therefore, the control of complex set of fields for 3D

radiotherapy is only possible with the use of an eventually unique dosimeter placed at the isocentre of the treatment.

The present paper proposes a review of recent progress in the field of in vivo dosimetry. A special focus is given on detectors that could be applied during the treatment itself to verify, as much as possible in real time, the dose received by the patient during a radiotherapy course.

## 2. Material and method

In this review, we look for the best solutions proposed to meet the needs of in vivo dosimetry for QA. The search has been performed on three different fields.

### 2.1. Technical devices

This section describes different technological approaches for radiation measurements, even if there are not available for in vivo use.

### 2.2. Clinical experimentation

The second section is a review of clinical use of implanted devices with consideration on anatomic and tolerance data.

### 2.3. Clinical use

The third section is devoted to a review of published series of patients treated with assessment of the dose by in vivo dosimetry; emphasizing the use of implanted dosimetry.

## 3. Results: a review

### 3.1. Technical devices

This section presents an overview of the dosimetry systems that can be used for in vivo measurements of the dose in anticancer radiotherapy. For different requirements of geometric measurements, there are one-dimensional or punctual, bi-dimensional and three-dimensional (volume) detectors.

#### 3.1.1. One-dimensional detectors

Most of the 1D detectors are based on either radioelectric methods (using ionization chambers or semiconductor devices) or radioluminescence principles (with scintillating materials).

**3.1.1.1. Ionization chambers.** It is a gas-filled cavity containing positive and negative electrodes that measures the amount of radiation passing through the cavity according to the quantity of electric charges obtained by the ionization caused by the radiation. Currently, the ionization chambers are used as reference to calibrate relative dosimeters in radiotherapy [20,23].

There are several types of the ionization chambers: the open air ionization chamber which is used by reference laboratories for the measurement of radiations, the cylindrical chamber used in the radiotherapy, and the flat chamber used in diagnostic

radiology and as monitor chamber in linear accelerators in radiotherapy.

Ionization chambers can hardly be miniaturized for patient implantation.

**3.1.1.2. Diodes.** A silicon diode dosimeter is a p-n junction semiconductor. These diodes are referred to as n-Si or p-Si dosimeters, depending upon the base material [21,32]. But, only the p-Si type is suitable for radiotherapy dosimetry, since it is less affected by radiation damage and has a much smaller dark current [21,26]. Diodes are used either in short circuit or in reverse bias mode where the junction current is proportional to the dose rate. The dose is obtained by integration of this current. Diodes are widely used for routine in vivo dosimetry, in particular for total body irradiation monitoring. They are provided with buildup encapsulation which must be chosen according to the type and quality of the clinical beam. Encapsulation also protects the diode from physical damage. Diodes are particularly useful for the small fields or high dose gradients area. They are also used for measurement of depth doses in electron beams. Diodes measure directly the dose distribution. Since silicon ( $Z=14$ ) is not tissue equivalent, the interaction of the radiations with the diode compared to tissues varies according to energy. Diodes also show a variation in dose response with temperature, dose rate, and angular incidence of the beam. Because of these dependencies, several correction factors have to be applied to the diode signal [22,31,36]. Diodes need frequent recalibrations for in vivo dosimetry [28,29].

**3.1.1.3. Metal oxide semiconductor field effect transistor.** The Metal oxide semiconductor field effect transistor (MOSFET) is a miniature silicon transistor which has an excellent spatial resolution, and offers very little attenuation of the beam due to its small size [13,33]. Irradiation generates electron-hole pairs within the gate oxide ( $\text{SiO}_2$ ) of the MOSFET. Charges trapped in the gate oxide, especially close to the  $\text{SiO}_2/\text{Si}$  interface, induce a shift of the device threshold voltage  $V_{\text{th}}$  which has been shown to be a linear function of received dose [21,33]. The main advantages of the MOSFET are the possibility of an instantaneous measurement and its small volume suitable for implantable dosimeters. MOSFET provides information on the accumulated dose, which cannot be reset. MOSFET exhibit small directional anisotropy ( $\pm 2\%$  for  $360^\circ$ ) and do not require dose rate corrections. However, its use is limited by the change of its sensitivity with the use, and its reduced lifetime (one can measure until 200 mV of cumulative signal which is equal to 70–200 Gy upon the precision mode applied). A study shows that the precision of the MOSFET is lower than that of the diodes (Precision 0.7% 1SD for MOSFET and 0.05% for the diodes) [27]. As the diodes, MOSFET exhibit temperature dependence, but this effect has been overcome by specially designed double detector MOSFET systems. Moreover, implanted devices are not subject to temperature deviation because of body thermal control. A study shows that the use of a micro-MOSFET as dosimeter in vivo for Intro operative external radio therapy (IOERT) is useful since its precision of 3.6% is enough for this type of treatment. The MOSFET's limited cumulative capacity of measure is not really

limiting for in vivo dosimetry but makes it even more expensive [16]. Another study shows that the achieved accuracy is lower than that of TLDs for medium X-ray energies used for superficial treatment in the range of 50 to 250 kV ( $\pm 5.6\%$  for the MOSFET and  $\pm 5\%$  for the TLD) [14]. The MOSFET was used as surgically implantable dosimeter in vivo in the USA in 2004 [34]. The system consisted of a P-channel MOSFET connected to microprocessor and a system of transmission of the signal by an antenna embarked in a glass capsule. This system makes 25 mm length and 3 mm thickness. This system was developed for a definitive implantation [34]. Another way to introduce the MOSFET in tissues is to use a brachytherapy catheter as for iridium implantations [24]. Presently, a micro MOSFET is commercially available from Thomson/Nielsen Ltd (Canada) for in vivo measurements for external radiotherapy and brachytherapy. The dimensions of this system are in order of 1 mm. This system was not designed to be used as implantable in vivo dosimetry device and remains expensive for a disposable use.

**3.1.1.4. Diamond detectors.** Diamonds have been used as in vivo dosimeter since 1987 [30]. Diamonds change their resistance upon radiation exposure. When applying a bias voltage, the resulting current is proportional to the dose rate. Diamonds can be used as very small elements which allow the measurement of dose distributions with an excellent spatial resolution. They are water equivalent, and resistant to the irradiation's damages. Their use is limited because of their energy dependence and their need of a preliminary irradiation before each use for polarisation effect reduction. They have temperature dependence in order of  $0.1\%/^\circ\text{C}$ . A study shows that diamonds don't have real advantages over diodes at the point of view of sensitivity and precision [12].

**3.1.1.5. Thermoluminescent dosimeters (TLD).** Thermoluminescence is a phenomenon of phosphorescence activated by heat. The luminescence signal is proportional to the dose received by the TLD material [18,20]. Lithium fluoride (LiF), mixed with a certain amount of impurities (Mg, Ti), is the most commonly used material for TLD [18,19]. Its density is considered as tissue equivalent. It is available as powder or in solid state (cubic,  $1\text{ mm}^3$  or rolls  $1\text{ mm}^2 \times 6\text{ mm}$ ). It has a good sensitivity with a large measurement dynamic ranging from  $10\ \mu\text{Gy}$  up to 1 kGy. However, it requires a calibration procedure before any use because of fading phenomenon. This fading precludes the use for cumulative dosimetry and consequently TLD needs immediate lecture by heating after each exposure that intrinsically reinitiate the dosimeter [18,20,23]. Therefore, the direct and continuous monitoring of the dose is not possible with TLD.

**3.1.1.6. Optically Stimulated Luminescence (OSL).** OSL is based on a principle similar to that of Thermoluminescence dosimetry, where light (from a laser) is used to release the trapped energy and to generate the luminescent emission. This dosimeter consists of a small chip of carbon-doped aluminium oxide ( $\text{Al}_2\text{O}_3:\text{C}$ ) coupled with a long optical fibre. This system offers a high level of precision and stability, with no dose rate dependence and mildly energy dependence [6]. The partic-

ular advantage of this system is that two signals are obtained: the radio-luminescence signal in real time during the treatment, and stimulation signal obtained after the irradiation by using a laser. A study shows that this system can be used with a high degree of accuracy (approximately 2%) like in vivo dosimeter for mammography [7].

**3.1.1.7. Plastic scintillator dosimetry system.** Plastic scintillators are relatively new development in radiotherapy dosimetry. The light generated in the scintillator during the irradiation is carried away by an optical fibre to a Photomultiplier tube (PMT) located outside the treatment room. The response of the scintillation dosimeter is linear within the range of radiotherapy doses. Plastic scintillation dosimeter can be made very small (about 1 mm<sup>3</sup> or less). They can be used in cases where high spatial resolution is required like high gradient dose regions, build-up regions, and small field dosimetry or close to brachytherapy sources. Dosimetry based on plastic scintillator is characterized by good reproducibility and long term stability. They are independent of dose rate. They have no significant directional dependence and don't need temperature and pressure corrections. [26] The main problem of these detectors is the noise produced in the light guide by Cerenkov radiation or fluorescence [8].

**3.1.1.8. Alanine/electron paramagnetic resonance dosimetry system.** Alanine, one of the amino acids, pressed in the form of rods or pellets with an inert binding material, is typically used for high dose dosimetry. The dosimeter can be used at a level of about 10 Gy or more with sufficient precision for radiotherapy dosimetry. The radiation interaction results in the formation of alanine radicals, the concentration of which can be measured using an electron paramagnetic resonance (EPR, known also as electron spin resonance) spectrometer. The intensity is measured as the peak to peak height of the central line in the spectrum. The readout is non-destructive. Alanine is tissue equivalent and requires no energy correction within the quality range of typical therapeutic beams. It exhibits very little fading for many months after irradiation [26]. A study shows that the accuracy of dose determination by EPR measurement was within the limit recommended of  $\pm 5\%$  for doses above 0.7 Gy [15]. The response depends on environmental conditions during irradiation (temperature) and storage (humidity). At present, alanine's potential application for radiotherapy is for dosimetric comparisons among hospitals.

### 3.1.2. Bi-dimensional detectors

**3.1.2.1. Portal imaging device.** This system gives a measure of the transmission dose through the patient. A matrix of "amorphous silicon" detectors are used to detect the treatment beams traversing the patient and form a 2D image. The Portal imaging detector is mounted on a motorized robotic arm, which allows it to be positioned with precise movements in the different directions. Portal imaging helps ensure treatment plan verification. Not just a port film replacement, Portal imaging can image and evaluate accuracy of delivery during the treatment course. It allows verifying the ballistic accuracy of the treatment plan

before any prescribed dose is delivered to the patient, and during subsequent treatment sessions. In particular, Portal imaging's ability to image during treatment allows verifying accurate positioning without increased dose to the patient. By a calibration to an absolute dose values, this system could be used as a system of in vivo dosimetry providing development, and certification could be obtained in the future. Promising works are already available on this particular use [11].

**3.1.2.2. Radiographic films.** Ionization of AgBr grains, as a result of radiation interaction, forms a latent image in the film. This image only becomes visible (film blackening) and permanent subsequently to processing. Optical density (OD), of the film is related to exposure to the radiation dose through a sigmoid dose-effect-relationship. The measure of optical density with devices called densitometers can give a measure of the dose providing to have calibrated the system for the conditions of use. Film gives excellent 2D spatial resolution and, in a single exposure, provides information about the spatial distribution of radiation in the area of interest or the attenuation of radiation by intervening objects. The useful dose range of film is limited and the energy dependence is pronounced for lower energy photons. The response of the film depends on several parameters, which are difficult to control. Consistent processing of the film is a particular challenge in this regard. Typically, film is used for qualitative dosimetry, but with proper calibration, careful use and analysis, films can also be used for dosimetry. Typical applications of a radiographic film in radiotherapy are qualitative and quantitative measurements, including electron beam dosimetry, quality control of radiotherapy machines [26].

**3.1.2.3. Radiochromic films.** Radiochromic film is a new type of film in radiotherapy dosimetry. The most commonly used is the GafChromic<sup>®</sup> film. It is a colourless film with a nearly tissue equivalent composition (9.0% hydrogen, 60.6% carbon, 11.2% nitrogen and 19.2% oxygen) that develops a blue colour upon radiation exposure. Radiochromic film contains a special dye that is polymerized upon exposure to radiation. The polymer absorbs light, and the transmission of light through the film can be measured with a suitable densitometer. Radiochromic film is "self-developing", requiring no chemical processing. Radiochromic has a very high resolution and can be used in high dose gradient regions for dosimetry (e.g. measurements of dose distributions in stereotactic fields and in the vicinity of brachytherapy sources). Dosimetry with radiochromic films has advantages over radiographic films, such as ease of use; no need for darkroom, film cassettes or film processing; dose rate independence; better energy characteristics (except for low energy X-rays of 25 keV or less); and insensitivity to ambient conditions (although excessive humidity should be avoided). Radiochromic films are generally less sensitive than radiographic films and are useful at higher doses, although the dose response non-linearity should be corrected in the upper dose region. Radiochromic film is a relative dosimeter. If proper care is taken with calibration and the environmental conditions, a precision better than 3% is achievable [26]. A study shows that the radiochromic film is the method of choice to measure the absorbed dose and dose

Table 1  
Comparison between the uses of different types of detectors.

Type of detector	Common use		Dependence on dose calculation	Independence on dose calculation	Remark and comments
	Reference, study, comparison	Daily practice			
Ionization chamber	*		*	* (\$)	(\$) To have a totally independent measure of the delivered dose using these methods, detectors have to be implanted in the patient's body or be placed at the axis at the entrance and exit of every beam. Thus for a treatment with n beams, 2n detectors would be needed to measure the exact delivered dose in a reasonable time, which is, however, complicated uneconomical and still time consuming
TLD		*	*	* (\$)	
Diodes		*	*	* (\$)	
MOSFET		*	*	* (\$)	
Diamante		*	*	* (\$)	
Optical fiber		*	*	* (\$)	
Plastic scintillators		*	*	* (\$)	
OSL		*	*	* (\$)	
Alanine dosimetry	*		*	* (\$)	
Portal imaging		*	*	* (£)	
Radiographic films	*		*		(£) If combined to any device giving the entrance dose, it could provide independent assessment of the dose Per se, these devices are only usable as exit checking of the beam and therefore cannot provide independent measure
Radiochromic films	*		*		Not "in vivo" but simulation close to the treatment reality
Gel dosimetry	*			*	
Implantable dosimetry in general		*		*	

distributions for high gradient vascular brachytherapy sources [4].

3.1.3. Three-dimensional detectors

3.1.3.1. Gel dosimetry system. Gel dosimetry systems are the only true 3-D dosimeters suitable for absolute dose measurements. The dosimeter is at the same time a phantom that can measure absorbed dose distribution in a full 3-D geometry. Gels are nearly tissue equivalent and can be moulded to any desired shape or form, using either Fricke solution (ferrous ions Fe<sup>2+</sup> that are converted into ferric ions Fe<sup>3+</sup> upon radiation exposure) or radiosensitive polymer gels.

However, these gel dosimeters could hardly be used as real in vivo dosimeters but they can be used for simulation to check complex or new treatment protocols before clinical application. It could even be imagined to use them for individual pretreatment, checking of complex 3D treatment plan without exit beams as charged particles therapy.

3.2. Clinical experimentation

The use of a micro-MOSFET as dosimeter in vivo for intra-operative external radiotherapy (IOERT) has proved useful, providing its precision is around 4 % [16].

The MOSFET has been first used as surgically implantable dosimeter in vivo in the USA in 2004 [34]. This system was developed for a definitive implantation [34]. The risk of mobility of the system from its initial implantation location has been observed in only one case upon 10 in early experience [35]. On the other hand potential complication could appear by definitely leaving this system in the tissues like infection or induce inflammatory reactions, although no such observation has been reported so far [10].

3.3. Clinical use

MOSFET have begun to be used as surgically implantable dosimeters and fiducial in regular practice in USA since FDA approval has been obtained for prostate cancer treatment [17]. A convincing experience has been recently published about 29 cases by Beyer et al. [10]. The used device is now commercially available from Sixel Technologies, Inc. [37].

4. Discussion and conclusion

4.1. Critical discussion of the review

The documentation and information sources of this review are very heterogeneous and cannot always clearly give the real state

Table 2  
Technical comparisons of the different types of detectors.

Type of detectors	Advantages	Disadvantages
Ionization chamber	Quick and stable Direct measurements Can be used as reference	Big volume Small efficiency Expensive
TLD	Small Good linearity at clinical dose region Low cost	Non instantaneous Fading Loss of sensibility with time Must be calibrated before each use
Diodes	Small Real-time measurement Low-cost	Not tissues equivalent Sensibility changes with temperature Directional effect Dependence on dose rate
MOSFET	Very small Instantaneous measure Memorize the dose Very good spatial resolution Small directional effect	Not tissue equivalent Very expensive Short life time (cumulative dose limit)
Radiographic Films	2D measure Good spatial resolution Permanent information Low cost	Not instantaneous Not linear Need to be calibrated before every use
Radiochromic Films	2D measure Good spatial resolution Don't need to be processed Tissue equivalent Permanent information	Very expensive Non instantaneous Needs a "radiological" environment
Portal imaging	2D measure Instantaneous Largely available Large development potential	Hypothetical use Low resolution Short life time
Diamonds	Tissue equivalent Resistant to damages No directional effect Small volume	Very expensive Need of pre-irradiation before use Dependence on energy
Optical Fiber	Low cost No directional effect Sensitivity and linearity	Bad spatial resolution Cherenkov effect (noise)
Plastic scintillators	Low cost Very small Good sensitivity Good spatial resolution Dose rate independent	Cherenkov effect (noise)
Optically stimulated luminescence	Low cost Stable No directional effects Dose rate independent	Cherenkov effect(noise) Needs of laser reading.
Gel dosimetry	3D measure Nearly water equivalent	Depend on temperature Diffusion needing quick reading MRI lecture Difficult to read Limited spatial resolution due to diffusion Not usable in vivo Time consuming
Alanine dosimetry	Tissue equivalent Little fading	Difficult to read Response depends on environmental conditions and storage

of use of the described methods. Others come from industrial advertisement sites and do not provide information on real use in regular practice [37], some other information are proposed as personal suggestions based on the availability of the technique in physics.

#### 4.2. Critical discussion of the reviews existing in this field

Presently, this field seems to remain mostly investigative with few general approaches proposed for clinical choice and application. We have been unable to find a recent review in accessible

publication on this field at the point of view of the clinical use. However, academic works as PhD reports have been found to provide some state of the art review in the recent years and, although difficult to find, they have been quoted in this review. [5,7] Of course some courses or textbooks provide some insight in this field but not, once again, at the point of view of the clinical use [26].

#### 4.3. Perspectives and arguments for an independent dosimeter for clinical practice

Finally, the needed information is in the tumor and therefore in the body of the patient. A critical point is to have an independent assessment of the dose delivered to the patient from the calculations and the modelization provided by the TPS. Moreover, if the information is obtained independently from the complexity of the ballistic of the treatment, it is to say from the number and the complexity of the beam arrangement it would be also a critical advantage. Ideally, only an internal 3D dosimetry modality would be perfect. However, as photon-therapy does not generate its proper signal in the patient's body, it is impossible to obtain such 3D information from a unique measurement, obtain from outside of the patient, and we cannot imagine to stuff the patient with punctual internal detectors. On the other hand, a direct measure of the internal absorbed dose to the isocenter, or at any point very close to the isocenter, of the treatment inside of the patient will give a truly independent assessment of the dose to that point. The combination of the measurement of the dose to this internal point, or a few critical internal points, and the verification by any device of the ballistic application of the treatment, still independently of the TPS modelization, would provide a thorough checking of the treatment.

The different technical possibilities could therefore be compared according to their characteristics of independence to the TPS dosimetry, the usefulness and the operability of the solution. Table 1 is an attempt of such a comparison.

#### 4.4. Critical comparison of the technical and practical characteristics of the different methods

As the table one shows, the different techniques are not equal at the point of view of their operability. The Table 2 gives a technical comparison between the different approaches which are usable to measure the delivered dose in radiotherapy. Drawn from Tables 1 and 2, it appears that two techniques of detection are interesting to be used as implantable systems.

The first is the semi conductors (diodes, MOSFET) which have good proprieties for in vivo measuring. But, to have a good electrical signal, the electronic module must stand beside the detector which will increase the volume of the implantable system. The MOSFET is very expensive and the development of a system based on these semi-conductors is very expensive also. Trials using these devices have been published [34,35].

The second is the optical methods based on scintillation fibers and optical fibers. These composites are not expensive and can be highly miniaturized. It is also tissue-equivalent and would worth

further development. Their main drawback is the Cherenkov light that is produced in the optical connection and gives some background noise.

However, this review showed that it is not possible to set up a real 3D internal checking of the dose distribution in the patient body. Thorough descriptions of the delivered dose in the patient, independently to the TPS modelization of the dose, combine:

- a central integrated dose measure obtained for instance at the isocenter by a miniaturized implantable dosimeter. This would provide a synthetic assessment of the treatment. A very high precision measurement will be needed to attract attention to any divergence;
- an external 2D measure of the delivered dose by the difference between the entrance and exit dose for all the beams use for the treatment session. Only a system born by the linac itself and intrinsically aligned with each beam could provide economically sustainable conditions for this second set of information. An adaptation of portal imaging device for this function could be a solution.

An intermediate situation could be the use of a set of implantable dosimeters located in different critical points of the treatment volume as the isocenter but also some organ at risk, which are the real limits of any radiotherapy. Only a simple, secure and economical system could be used for that.

Such a perfect dosimeter is still not available. However, some interesting approaches as implantable MOSFET dosimeter exist. Ideally, such a dosimeter should have the following characteristics: have a high accuracy, be safe (no electronics/high voltage close to the patient), have a small size and a shape fully acceptable by the patient (not aggressive, easy to fix, immobile, tissue compatible. . .), have no or few dependencies on beam parameters, provide the absorbed dose in real-time, be universal (able to function in both photon and electron beams), be easy to use and calibrate, be detectable in the anatomic volume to check its position, and not expensive for disposable use of its implantable part.

#### Conflicts of Interest

The authors declare that they have no conflict of interest.

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