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Preliminary investigation of performance of thermoluminescent dosimeters for dose verification in brachytherapy

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Summary. — Brachytherapy represents the treatment of choice for many cancerous lesions, including skin tumours. Purpose of the study was to investigate the performance of thermoluminescent dosimeters of type 100, (TLD-100), for dose verification in high dose-rate treatment with a radioactive source of iridium-192. A set of TLDs-100 was calibrated with a 250 kVp X-ray beam in the dose range 0–5 Gy. Through a head and neck phantom, TLDs were fixed on districts corresponding to volumes of interest, including the target volume and some critical structures, then a single fraction of brachytherapy treatment was delivered. The dose measurements provided by TLDs were compared with the planned ones and the results were discussed in the light of limitations affecting the *current treatment* planning systems and critical aspects relating to brachytherapy implementation that still occurred in clinical settings. The findings of the study allow us to conclude that TLDs-100 show a good performance in the radiation field investigated and the use of so small, cheap and practical dosimetry system is potentially an optimal strategy of improving and standardizing the quality assurance protocol in brachytherapy.

1. – Introduction

Brachytherapy (BT) alone or in combination with external beam radiotherapy (EBRT) and chemotherapy is an appropriate and effective treatment option for curative management of cancers in a variety of disease sites. Basically, BT is used for the

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treatment of cervical, prostate, bosom, skin disease, gynaecological malignancies, breast and prostate cancer [1]. The physical principle of BT lies in the use of photonic or particle energy coming from the decay of radioactive isotopes located in the tumour (interstitial BT) or in its immediate proximity (superficial BT), allowing to deliver a very high radiation dose directly to the tumour, close to the sources, limiting the radiation exposure of surrounding healthy organs and tissues [2,3]. A more precise dose deposition within the tumour mass and a higher concentrated radiation dose compared to EBRT improve the local tumour control minimizing the probability of side effects in the organs at risk (OARs) at the same time. For this reason, BT is an optimum tool in cases of irregularly shaped anatomies or unfavourably located cancer, such as in the head and neck or lower limbs, where critical structures are often proximal. For patients with small shallow lesions (face skin, near eyes and nose) or large lesions, which cannot be surgically removed due to the failure of previous surgery or other comorbidities, a well planned BT is often the gold standard treatment providing excellent cosmetic outcomes [4-6].

Throughout the mid-20th century a continuous increased use of BT modality has occurred mostly for surface lesions which is the most common malignancy affecting globally 2–3 million people each year, as declared by the World Health Organization (WHO) [7,8].

Despite major advantages of modern brachytherapy such as the use of 3D image-based treatment planning systems (TPSs), the implementation of imaging in BT target and OAR definition, several errors and uncertainties still occur during the many steps of treatment planning and delivery, affecting the clinical result. Uncertainties in delivered dose depend on CT imaging quality, which affects the accuracy of the reconstruction of patient clinical structures and catheters in the implant, accuracy of the TPS algorithm and both source calibration and positioning. The main sources of uncertainties affecting the planned dose distribution originate from the accuracy of the source calibration [9] and the dose calculation algorithm incorporated in most of the TPS used to date. The formalism, introduced by the American Association of Physicists in Medicine (AAPM) Task Group (TG)-43, assumes that the patient is made of water neglecting tissue heterogeneities and intersource dose attenuation [10]. Furthermore, another major source of uncertainty affects the accuracy of dose delivery that is the organ applicator movements between imaging and treatment delivery stages [11-13]. A detailed description of the most frequently occurred errors in BT is reported in the International Commission on Radiological Protection (ICRP) Report Nos. 86 [14] and 97 [15] as well as IAEA safety report series 17 [16].

Although Institutions should have a commissioning and BT quality assurance (QA) program in place as recommended by the AAPM [17, 18] in order to ensure the accuracy, efficacy and safety of the patient treatment, independent and patient-specific dose verification is not performed systematically. On the other hand, currently, no guidelines available from the AAPM discuss the breadth and standard of care for surface brachytherapy in detail [19]. Clinical aspects of treatments of skin cancers with brachytherapy sources are addressed by the American Brachytherapy Society (ABS) [20] and the Groupe Européen de Curiethérapie-European Society for Radiotherapy and Oncology (GEC-ESTRO) [21] with the aim of promoting quality and standardization of clinical procedures.

In this framework, *in vivo* dosimetry (IVD) may have a potential role in outlining a significant number of treatment errors, thus also implementing the treatment procedure accuracy. Recently Fonseca *et al.* [22] have summarized the types of deviations between delivery and treatment plan that can occur in brachytherapy and identified errors that could be identified by IVD.

Due to the innovations and development of new BT treatment approaches, over the last decade an increasing number of researchers have been interested in the issue of dose monitoring and verification in brachytherapy, as demonstrated by the wide available literature works [1, 22-27]. Some authors analysed the state-of-the-art methods and the challenges typical for BT dosimetry and investigated the performance of several dosimeter devices today suitable for IVD in medical physics dosimetry [27-29]. Although no single method can be considered ideal for the dosimetry of brachytherapy sources, thermoluminescent (TL) dosimetry, a well established tool for dose verification in many clinical radiotherapy settings, is the most commonly employed tool for verifying dose distributions around radioactive sources for brachytherapy [30]. Thermoluminescent dosimeters (TLDs) exhibit favourable physical and dosimetric properties for IVD dosimetry: TL response is linear over a wide range of doses used in radiotherapy, they can be reused after annealing, the high sensitivity allows measurements at both low doses and low dose rates, they are small enough to be placed in patient body cavities if properly encapsulated and sealed for insertion into catheters allowing high-precision dose measurements. Furthermore, TL material is approximately tissue equivalent (effective atomic number of 8.2 similar to 7.4 for tissue) so that the interaction phenomena are comparable with those occurring in patient's tissues.

Among a wide choice of TLDs, lithium fluoride (LiF) type was established as the most reliable detector for BT absorbed dose measurements by the Interstitial Collaborative Working Group (ICWG) [31] and more recently by the AAPM TG-43 [10, 32].

The present work is a preliminary investigation of the potential of thermoluminescent dosimeters in estimating the effective dose delivered in high dose-rate (HDR) brachytherapy with 192-iridium (192-Ir) source for skin lesion treatment. To this aim a set of LiF:Mg, Ti TLD type (TLD-100) was characterized and calibrated with X-ray beam at a tube voltage of 250 kVp and subsequently exposed to a single treatment fraction of BT simulated on an anthropomorphic phantom.

The goal of this dosimetric study was to measure the dose absorbed by the clinical target volume (CTV) and critical organs and tissues (eyes and brain) and then assess any discrepancy between the planned and measured dose.

2. – Materials and methods

2˙1. *TLD dosimetry and calibration.* – A total of 36 TLDs-100 supplied by Harshaw Chemical Company (sensitive volume $3.2 \times 3.2 \times 0.89\,\mathrm{mm}^3$) and marked with an identification number at the first use were employed for the study. TLDs-100 underwent a pre-irradiation annealing cycle in air of 1 h at 400 °C followed by 2 h at 100 °C to clear the low-energy traps. Then, TLDs were cooled to room temperature where they remained for at least 24 h before use [33]. A standard version of the Harshaw TLD model 5500 hot (nitrogen) gas reader installed at the Laboratory of Radioactivity (LaRa), Department of Physics of the University of Naples Federico II, was used for the automatic reading of the dosimeter signals. The same time temperature profile was used to read each TLD. Read-out was performed integrating TL light from 100 °C upwards using a heating rate of 5 °C/s up to a maximum temperature of 300 °C (40 s total integration time). The TL signal released in the region between 50 and 150 °C, corresponding to the plateau regions of the heating profile, was stored as TL measure.

The calibration of the TLD batch was performed in the dose range 0–5 Gy with a 250 kVp X-ray Siemens tube installed at Department of Physics of the University of Naples Federico II for experimental aim. TLD chips in groups of ten, eleven and twelve,

were placed one by one in a Petri dish at the isocenter plane and irradiated sequentially at 0.5, 1.5, 5 Gy (fig. 1). Three dosimeters were not irradiated but used to measure the background signal. Then, the average TL signal (corrected for background) of the TLDs for each dose group was determined. The Calibration Factor (FC) was defined as the inverse of the tangent of TLD absorbed dose response curve. This factor allows the dosimeter response, that is, the TL signal in coulomb after irradiation, to be converted to the received dose according to the following equation:

$$\text{Dose} = \frac{\text{FC}}{\text{TL}}. \tag{1}$$

2˙2. *Treatment planning and irradiation experiment.* – A brachytherapy treatment planned for a skin lesion localized on the skull (head and neck tumour) was delivered on an anthropomorphic phantom. A single fraction of 3.5 Gy was prescribed on the CTV. The irradiation experiment was performed at the Radiotherapy Unit of the National Cancer Institute IRCCS Fondazione G. Pascale in Naples, equipped with the TPS Nucletron Oncentra® Brachy v4.5.3 and Flexitron® brachytherapy afterloading platform (Elekta, Stockholm, Sweden) containing the 192-Ir source.

The CT-based planning was elaborated on an anthropomorphic head and neck phantom that mimics well the patient tissue, optimizing the dose on the clinical target volume and region of interest previously contoured on CT slice images. The protocol for brachytherapy dose calculations implemented in Oncetra Brachy TPS was based on dose

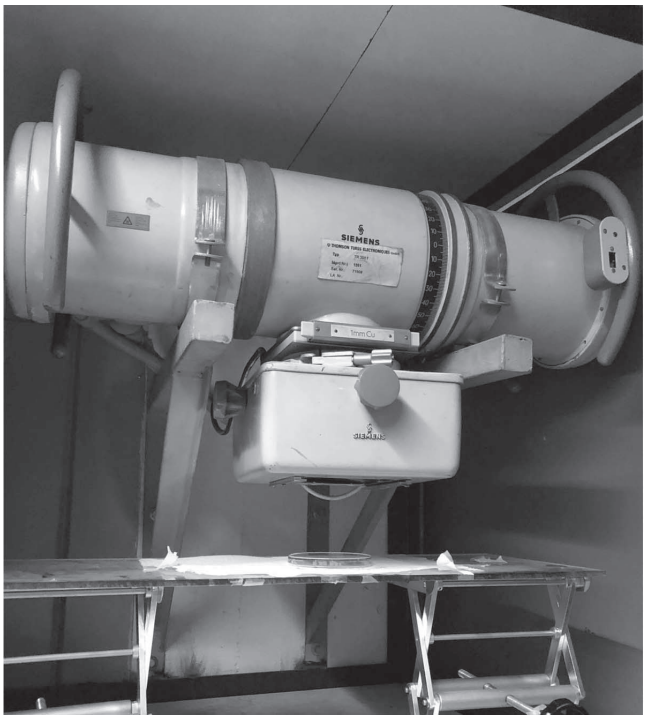

Fig. 1. – Picture of the Siemens X-rays tube with TLDs accommodated in the Petri dish for irradiation.

formalism defined by AAPM TG-43 [10]. As the final step of the BT planning workflow, TPS provides the sources positioning in relation to the target volume and other anatomic characteristics of interest associated to the best dose distribution outcome.

Nineteen TLDs were fixed on the district of interest according to the following distribution scheme: eight on CTV, five in the brain, three on the left and right eye. The remaining TLDs were used for the background measure. Figure 2 shows the head and neck phantom with TLDs fixed in the brain (left panel) and on the eyes and CTV (right panel). BT treatment was delivered by keeping the sources staying at designated dwell positions for programmed amounts of time, according to the planned position schedule.

The radioactive source is stored in the Flexitron, a computer-controlled medical device equipped with a source drive mechanism for moving the source into treatment positions within an applicator. A channel selector mechanism allows choosing one out of 40 treatment available channels. In order to perform the irradiation, the 192-Ir source was transported through seven channels coupled to as many guide catheters along a plastic portable mask designed on purpose. Before accommodating the mask on the skullcap of the phantom, the mask was tied with a lace to avoid any movement. Figure 3 shows the mask fixed on the skull (left panel) and Flexitron with the source channels transported via catheter to the phantom (right panel).

2˙3. *Statistical analysis*. – Data analysis was performed using the Excel package of Microsoft Office 365 ProPlus. The calibration curve was obtained by linear fitting of TL-dose points. Goodness of the fit was evaluated by the R^2 coefficient. The calibration coefficient was carried out from the slope of the curve with its own statistical error. The mean value of dose measurement corresponding to TLD group for each district was calculated and statistical error was provided by standard deviation.

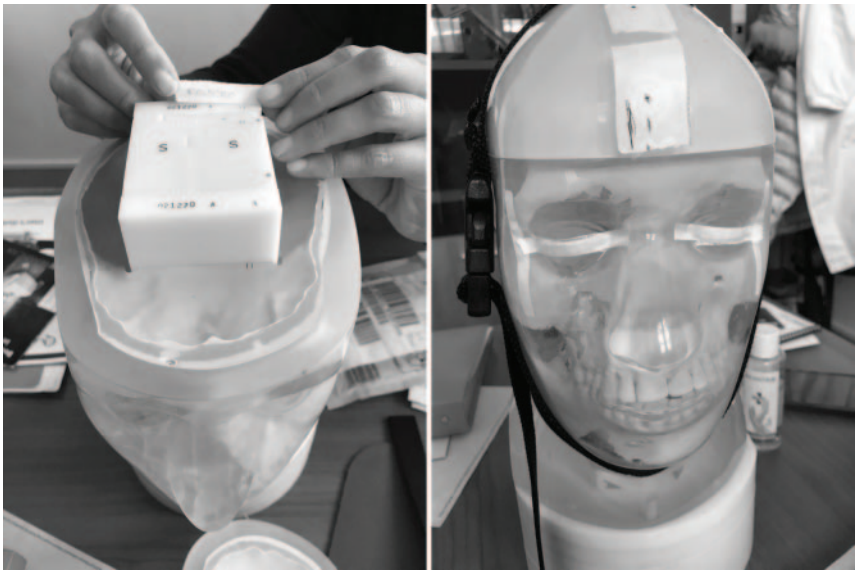

Fig. 2. – Picture of the head and neck anthropomorphic phantom with TLDs fixed in the brain (left panel) and on the eyes and skull (right panel).

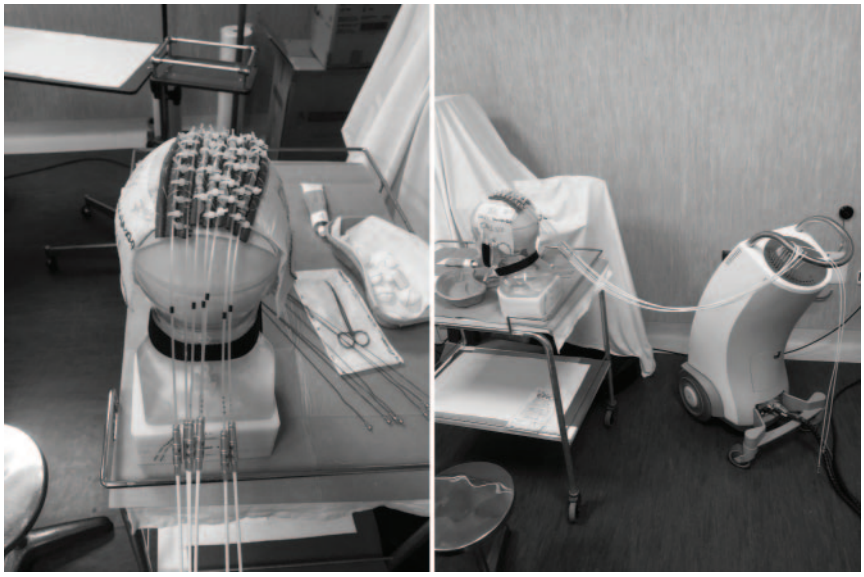

Fig. 3. – Picture of the mask fixed on the skull of the phantom (left panel) and Flexitron with the source channels transported via catheter and fixed on the mask (right panel).

3. – Results and discussion

The linear fit of the dose-response points resulting from TLDs exposure in 250 kVp X-ray beam for calibration in the dose range 0–5 Gy was reported in fig. 4.

The results of linear regression analysis show a very high R^2 value close to one ($R^2 = 0.9999$), demonstrating that the calibration curve is linear in the dose range of interest. The slope of the linear equation reported in fig. 4 provided the following value of the calibration factor:

$$\text{FC} = 5.10 \pm 0.04 \ \mu\text{C/Gy}. \tag{2}$$

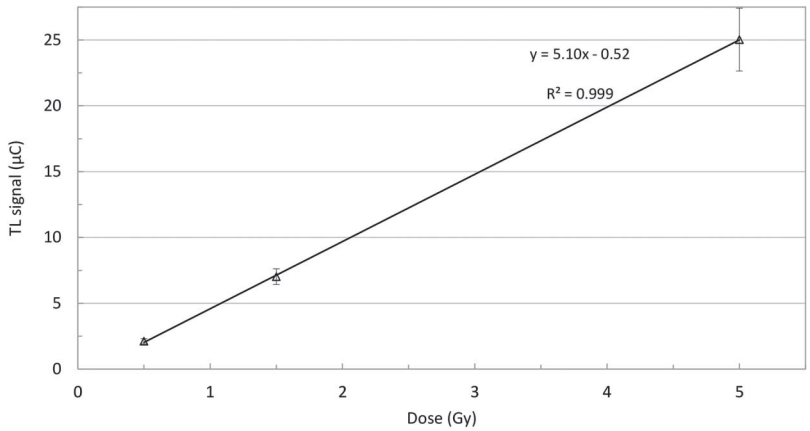

Fig. 4. – Calibration curve and linear equation of thermoluminescent dosimeters (TLDs) exposed to 250 kVp X-ray beam in the dose range 0–5 Gy. R = correlation coefficient.

TABLE I. – *Mean dose value and corresponding standard deviation of thermoluminescent responses of TLDs-100 exposed in each volume of interest.*

Volume	Dose $\pm$ δ Dose (Gy)
CTV	4.1 ± 0.2
Brain	0.81 ± 0.05
Right eye	0.063 ± 0.004
Left eye	0.059 ± 0.004

The obtained linear trend is in accordance with the TL response behaviour well assessed in many literature works according to which TLD-100 chips have a broad practical linear dose range, from a few cGy to approximately 10 Gy for beams of quality and energies useful for applications in radiotherapy [34-36].

The mean dose values computed from TL responses of TLDs for each volume of interest were reported in table I.

In order to evaluate the dosimetric performance of TLDs the dose volume histograms provided by the TPS for CTV and structures considered at risk must be briefly discussed. The planned dose was optimized to CTV according to dose-volume parameters. In fig. 5 the dose volume histograms (DVHs) of CTV and healthy organs and tissues are reported. The dose for CTV was planned so that the 90% of target volume received at least 87% of the prescribed dose, corresponding to a dose of 3 Gy. The maximum dose received by CTV resulted equal to 140% of the prescribed dose, corresponding to 4.9 Gy. A dose

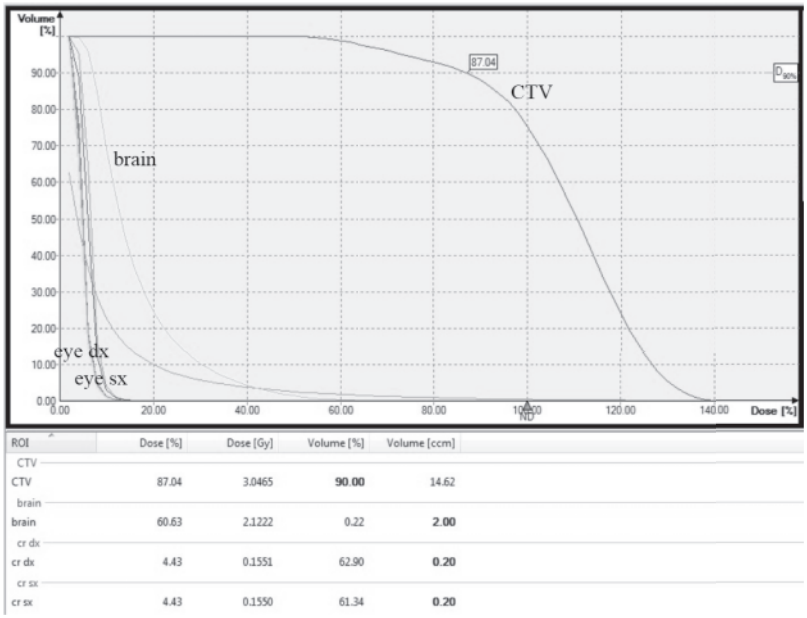

Fig. 5. – Dose volume histograms (DVHs) of clinical target volume and organ and tissues at risk (eyes and brain) involved in the study.

limit of 150% of the prescribed dose was set on the skull during the planning phase in order to avoid radiation-induced burns.

As shown in table I, the mean dose received by the CTV, carried out from TLDs reading, resulted to be 117% of the planned dose to the target volume with a narrow standard deviation. Since dose distribution on the target achieves good homogeneity, we can speculate that CTV was adequately treated. Unfortunately, when dealing with OARs DVH analysis results weak, since BT techniques implement significant dose escalations between target and surrounding structure as evidenced by the rapid fall of DVH in OARs (see fig. 5). 2-dimensional DVH disregards any spatial dose distribution information and regional dose inhomogeneity, as a consequence the average dose measure on a selected region of the volume of interest resulted no more representative of the total absorbed dose. Dose inhomogeneity was probably indirectly detected through the large standard deviation found in dose measurements in the brain, where TLDs covered a small volume fraction. In addition, since brachytherapy dose distributions are significantly inhomogeneous and characterized by high dose gradients, IVD for target and critical structures dose verification suffers from the particular challenge of precise detector positioning in high-gradient fields.

In addition to the limitation of the tool available to assess some deviation between planned and measured dose, intrinsic uncertainties in the dose measurement method must be considered too. First of all, because of the energy dependence of TLD [37-39], a significant impact on the measure of the effective absorbed dose could derive from calibrating TLDs using a 250 kVp X-ray beam whereas the brachytherapy irradiation was performed with a 192-Ir source emitting gamma photons with mean energy of about 360 keV.

On the other hand, the Oncentra TPS, which incorporates the AAPM TG-43 [10, 18] formalism, presents the limitation of calculating the dose distribution basing on the interaction model of radiation in water neglecting the non-water equivalence of the phantom materials. This approach leads to a theoretical error in the dose outcome, since point dose calculation depends on the mass attenuation absorption coefficients of the material interacting with radiation in that point. The approximation of the phantom material as water in the calculation affecting actual TPSs routinely used for BT represents one of the limiting factors for dose comparison between dose distribution provided by TPS and *in vivo* measurement [40]. In this context, the obtained dose in brain could be overestimated by TPS because the attenuation of the radiation by bone and muscle structures present between the source and the TLDs is greater than that by water. On the eyes, the mean dose measured by the TLDs resulted to be 0.06 Gy, lower than the dose computed by TPS equal to at least 0.15 Gy to the 60% of the total volume, as shown by the dose volume histogram (see fig. 5).

Since the correlation between radiation dose and normal tissue complication probability is well assessed by findings of many literature works [41-47], independent verification of treatment delivery is particularly important in high–dose-rate BT in which large doses per fraction (>5 Gy) were prescribed, which means that the consequence of a fractional error may lead to severe adverse complications to OARs. Sure, IVD may contribute to more precise dose reporting [48], especially for the OARs. In particular, IVD on skin is of relevance during the treatment of head and neck cancer since the skin is an OAR close to the treated volume and has significant dose calculation uncertainties [10].

Eye lens represents a critical structure since the high radiation sensitivity can lead to radiation-induced lens changes or visual disability requiring cataract surgery. With regard to the induction of deterministic effect on the eye lens, in recent years, the

International Commission on Radiological Protection (ICRP) in Publication 118 [49], based on epidemiological evidence [50-52], revised dose threshold for cataract induction, establishing a limit of 0.5 Gy, compared with the previous threshold doses for visual-impairing cataracts of 5 Gy for acute exposures and >8 Gy for highly fractionated ones. This revised dose limit is incorporated into the European Council Euratom Directive [53] for occupational exposure recently transposed in the national regulation [54]. The reduction of the limit for occupational exposure for the lens of the eye has significant implications not only for employers and workers, but also for patients in relation to organs and structures not involved in the radiation treatment for which a dose "as low as reasonably achievable" must be achieved. In the perspective of the radioprotection issue for the patient, the dose to eye lens resulted to be much below the cut-off for radiation-induced cataract (<0.5 Gy).

This study gives a new insight on a series of issues related to the *in vivo* dosimetry in BT, currently limited in many departments due to difficulties and complexities, in particular due to challenges of the high-gradient BT dose distribution and the large range of dose and dose rate applied. The work represents a preliminary evaluation of the performance of TLD in the field of BT. A more accurate calibration, compliant with the radiation source used for BT delivering, will allow to obtain a more reliable dose value measurement. In addition, we plan to perform a large amount of dose points measurements in order to obtain a more representative dose distribution especially in the organs at risk.

The obtained results encourage planning further investigation on the feasibility to use thermoluminescent dosimetry in BT since they are well established dosimeters in clinical practice, easily to handle and cheap, characteristics which are useful to achieve a standardized protocol for BT treatment verification.

4. – Conclusions

The goal of the study was to investigate the feasibility of using TLDs-100 for dosimetry in brachytherapy. The doses measured by TLDs after a simulated high dose-rate BT treatment for skin lesion on a head and neck phantom are comparable with the expected ones within the uncertainties still affecting the accuracy of dose delivery in the BT technique. Although several improvements are necessary to implement a dosimetric QA protocol in brachytherapy, the results of the work support further research in this field in order to include thermoluminescent dosimeter for standard use in clinical routine to guarantee the safety of a widely applied radiotherapy treatment.

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