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Characterization of a detector for β^- radio-guided surgery

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Summary. — This paper reports a new device for the radio-guided surgery technique exploiting β^- emitters. A specific intraoperative β^- detecting probe based on a low-density organic crystal, the diphenylbutadiene-doped para-therphenyl, coupled by optical fibres to a photomultiplier, was developed. A portable readout electronics was designed to provide the surgeons with multi real-time feedback. The aspects related to the applicability of the device, in particular the perception of the spatial resolution of the probe and the comprehension time necessary to the operator to interpret the system response were investigated. Preliminary promising results support the possibility of using this innovative probe in cancer surgery.

1. – Introduction

The precise identification of tumor remnants after the resection of the bulk mass may be difficult for the surgeon. Even if clear clinical images (PET or MRI) can define its position and boundaries, the tumour may slightly change its position during the surgery. A huge number of techniques were developed to assist the surgeon in this aspect. One of these is the radio-guided surgery (RGS) [1]. In this technique a radio-marked tracer

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is administered to the patient before the operation. A radio-marked tracer is a chemical compound in which a decaying radioisotope replaces one or more atoms. The tracer is preferentially taken up by the tumor cells, increasing the radioactivity of the tumour with respect to the surrounding healthy tissues. Radiations can be detected during the surgical procedure, allowing to localize the tracer and consequently the malignant tissue. After the tumour masses removal, this technique can successfully identify the tumour remnants (up to 0.1 ml of volume) in real time, volumes otherwise invisible by the naked eyes.

Nowadays radio-tracers marked with ^{99m}Tc, a gamma emitter, are widely used. This isotope generates photons with an energy of 140 keV, meaning that, considering the density of the human body, their path inside the patients is in the order of the decimetre. This implied that RGS could be used only in those cases where the radiation originated from the tracker uptake of the nearby healthy tissue does not constitute a significant background to the measure. Our proposal is to use β^- decaying isotopes instead of gamma emitters [2] exploiting their lower penetration power (less than 1 cm for electrons with energy of the order of MeV). With this approach RGS could be extended, for example, also to brain and abdomen tumors, and to paediatric tumors. At present we are studying the potential of the DOTATOC, a somatostatine analogue, marked with ^{90}Y in brain tumour clinical applications (meningiomas and gliomas [3]).

2. – The detector

A β^- probe was created for the detection of low-energy electrons (fig. 1). An organic crystal, para-terphenyl doped with 0.1% diphenylbutadiene, was used for its high sensitivity to e^- and its scarce sensitivity to γ [4]. The crystal shape was a cylinder of 5 mm in diameter and 3 mm in height encapsulated into a black PVC ring with external diameter of 11 mm. The light tight was ensured with a 10 μm thick aluminium foil. This assembly was mounted on the top of an aluminium cylindrical body (diameter 8 mm and length 14 cm). The scintillation light produced by electrons crossing the small crystal was guided by four 50 cm long optical fibres to a Hamamatsu H10721-210 Photo-Multiplier Tube (PMT). The output signal is then processed and converted by a custom electronics in counts per seconds displayed on a remote monitor. The choice of this module was driven by his low input voltage, 5 V. This avoided the use of high voltage in proximity of the patients, maximize the compatibility of the device. With this configuration the device resulted insensitive to electrons with an energy lower than 487 ± 33 keV.

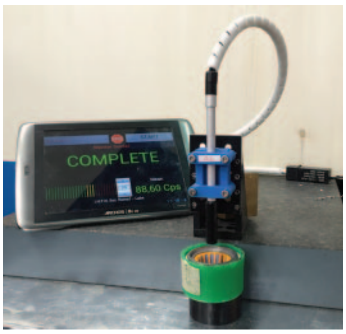

Fig. 1. – The probe described in this article. The white wire acted as protection for the four optical fibres that were located inside. In the picture also the PMT and the display are shown.

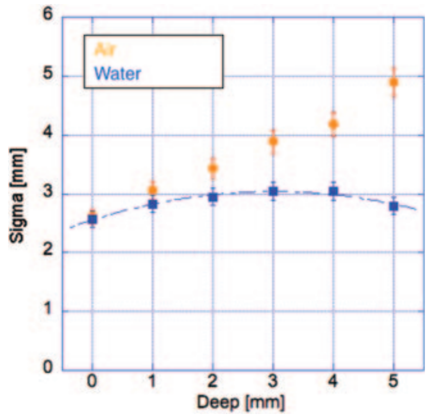

Fig. 2. – The yellow/blue dots/squares represent the sigma of the Gaussian profile obtained in air/water as a function of the depth in water.

This device's energy cut was compatible with ^{90}Y energy spectrum, since its mean value was 950 keV.

3. – Operation tests

The probe performances were studied in laboratory using sources of ^{90}Sr and ^{90}Y. These tests allowed to understand the new surgeons' perceptions of the field and to best assist them in the search for tumor residuals.

3˙1. *Spatial resolution*. – A scan over a point source of ^{90}Sr was performed fixing the probe to a two-axis motorised system. The linear actuators had a precision of 1.5 μm. The profile of the sources was reconstructed collecting measure in 10 s/position with steps of 1 mm. Scans were made in water and air, changing the distance between the probe and the source. Scans in water, given the approximation between human body and water, were used to evaluate the discovery potential in real cases. In fig. 2 the sigma of the Gaussian profiles obtained in water (blue) and air (yellow) are shown as a function of the depth in water. Whereas in air sigma increased with the distance due to geometry, in water this effect was mitigated by the absorption power of the medium. In fact, independently of the deep of the source, sigma was found to be equivalent to 3 mm. This is the maximum distance from which the probe was able to identify a point size residual during the operation.

3˙2. *Human feedback*. – The scope of the present work was to investigate the average time that effectively an operator needs for the interpretation of the device's answer. Specific phantoms reproducing tumour remnants embedded in healthy tissue were created to simulate the expected signal-to-noise ratio of real clinical cases. The phantoms were made of commercially available sponges (Wettex Classic by *Vileda*®) filled with ^{90}Y in saline solution.

To simulate a 0.05 ml tumour residual surrounded by healthy tissue, a small cylinder (SC) — 5 mm diameter, 2.5 mm height— was inserted into a larger torus (LT) with the same height and external diameter of 20 mm. Different signal-to-noise ratios between the tumor and the surrounding healthy tissue were obtained changing the dilution of the

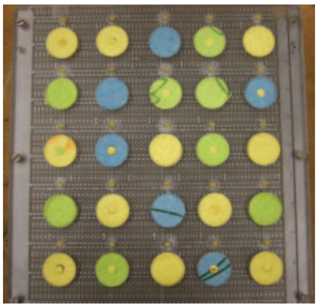

Fig. 3. – The board filled with the phantoms.

^{90}Y solution. A nominal ratio of one to ten, the worst uptake of DOTATOC in case of meningioma, was used for this test [3].

The minimum time that a human tester needs to comprehend the device answer was estimated building a specific set-up. Twenty-five phantoms were randomly inserted into a plastic board (matrix of 5×5) (fig. 3 and 4). The different combinations considered are reported in the following list:

- 5 SC activity 0 - LT activity 0
- 5 SC activity 1 - LT activity 1
- 5 SC activity 10 - LT activity 0
- 10 SC activity 10 - LT activity 1

A led driven by a microprocessor (Arduino mega board [5]) was fixed over each position. The software choses randomly one led and turns it on for a fixed time (we investigated the range 1–5 s), then turns it off. During the same period a human tester must check if the internal phantom was filled with high or low activity, deciding to remove or leave it. The decision was hence based on the rate on a phantom with low activity acquired at the start of the scan. The process went on until all positions, avoiding repetitions, were inspected.

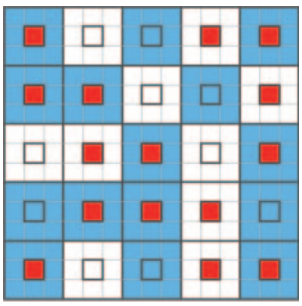

Fig. 4. – Representation of phantoms' activity. Red indicate an activity of ten, blue of one, and white zero activity.

The testers were equipped with different feedbacks: numeric (the tablet), visual (a blinking led) and acoustic (a buzzer). The feedbacks were related to the rate acquired; for example the blinking frequency changed according to the count for second. Independently of the feedback supplied, no operator was able to take a decision in less than 2–3 s, with a bit more time all of them detected all the hot spots.

4. – Conclusion

A new probe to detect β^- decays was developed for surgery application, extending the field of application of RGS to different families of tumors.

The probe was designed to identify residuals with a minimum volume of 0.1 ml, although extrapolating our results, we estimated that residuals smaller than the diameter of the probe, independently of their depth, are seen large 3 mm. This area of resection is compatible with the limits of surgical operations, since it is well below the minimum volume that can be removed for technical reasons.

The minimum time that a human tester needs to comprehend the device answer, independently of the assets, resulted to be ~ 5 s. This time results to be well above the time estimated necessary to individuate the residuals, that for this probe and for the case of interest is in the order of the second [3]. In conclusion, this paper confirm the results of our previous studies [2, 3]. The characteristics of our β^- decays probe are promising. It can become a valid diagnostic tool for the surgeons, supporting them in the precise and objective recognition of residuals thus shortening their decision time on how to proceed during the resection, improving the general performance of the operation in a highly conservative way thus making it fit for the purpose.

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