



## A computational dosimetry tool for the study of tumor doses and skin toxicities in BNCT

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### ABSTRACT

A Matlab-based computational tool, named SPHERE, was developed that helps determining tumor and skin doses in BNCT treatments. It was especially designed for cutaneous melanoma treatments and, among its features, it provides a guide for the location and delineation of tumors and a visual representation of superficial dose distributions (for both tumor and normal tissues). It also generates cumulative dose–volume histograms for different volumes of interest and dose–area histograms for skin. A description of the tool is presented, as well as examples of its application.

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### 1. Introduction

The Comisión Nacional de Energía Atómica of Argentina (CNEA) and the oncology center Instituto Ángel H. Roffo initiated the phase I/II clinical trial of peripheral melanomas in 2003 (González et al., 2004). Since then, a total of 7 patients with 88 nodular lesions in 10 anatomical areas were treated using the hyperthermal neutron beam of the RA-6 reactor at the Centro Atómico Bariloche (Menéndez et al., 2009). During these years, natural difficulties and questions regarding tumors and normal tissues were raised.

One of these questions was how to determine doses in small tumors that could not be delineated in medical images. About half of all lesions treated in Argentine clinical trials had a superficial diameter lower than 5 mm. Additionally, tumor and normal tissue mass densities are very similar, so that their gray intensity levels in CT images are not very different. Thus, the contrast between tissues is very poor and this makes it very difficult, if not impossible, to locate those nodules with small size in computed tomography (TAC) images.

Another question, of a more general nature, was how to prescribe the dose in normal skin to deliver a safe treatment while imparting doses sufficient to control tumors when dose distributions are very inhomogeneous (inhomogeneities up to 50% in 100 cm<sup>2</sup> of skin can be found in CNEA treatments).

These concerns motivated the development of a computational tool that helps guide physicians through location and delineation of tumors in medical images and, when this is not possible, provides an estimation of the dose delivered to the nodule. Moreover, it allows the study of normal skin dosimetry by computing cumulative dose–area histograms and specific figures of merit that cannot be obtained with the routinely used treatment planning system. In this work, we present the main features of the developed computational system and show some examples of its use. The applicability and usefulness of the new tool SPHERE to other treatments are also discussed.

### 2. Materials and methods

The system was programmed in Matlab (The MathWorks Inc.), using the graphical user interface capability. It is built on multiple windows devoted to different purposes. Although at present it runs under Matlab, a stand alone version of the program is planned.

As a first step, the user loads the input data involving medical images, parameters relevant to the treatment plan evaluation, and calculated physical doses (such as those generated by MCNP with NCTPlan model) (González et al., 2002, 2005).

For tumor location, only a picture and medical images of the patient's anatomy are needed. Based on CT images, a 3D reconstruction of the patient anatomy is built (see Fig. 1).

In order to facilitate location and delineation of tumors, a registration of the 3D reconstruction and a picture of the anatomy can be performed by means of the fiducial markers used for

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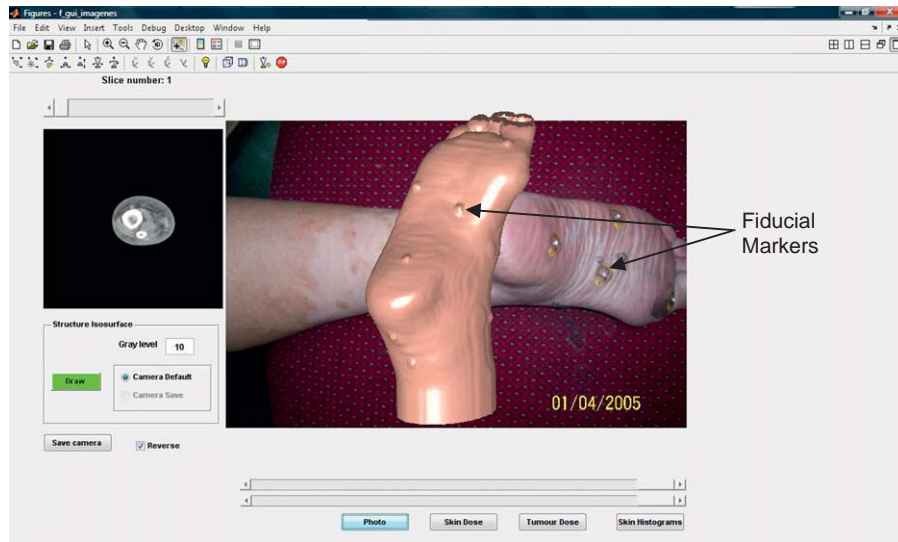


Fig. 1. Reconstruction of the patient's anatomy based on the TAC images.



Fig. 2. Registration of the 3D reconstruction and the corresponding picture of the patient's anatomy.

treatment planning purposes. Reference marks appear both in the TAC images and in the photograph of the anatomy (see Fig. 1).

Since transparency of the 3D reconstruction is controlled by the user, they can be used as registration points to achieve a good superposition (Fig. 2). The registration is carried out by means of rigid movements (rotations, translations and dilations) of the 3D reconstruction. In some cases, a minor correction in the 3D aspect ratio is needed (of about 1 or 2%). After the registration, the transparency of the 3D reconstruction can be increased to start delineation. The physician points the cursor directly on nodules in the picture, as shown in Fig. 2. Since the 3D reconstruction is superimposed onto the picture (although not necessarily visible), the physician is actually establishing the coordinates of some points of the nodules in the CT study. Then, the program identifies the TAC slices corresponding to the selected tumors and shows on each slice the physician selected points (for example in Fig. 2, the yellow dot that appears automatically in the corresponding CT slice when the user points the cursor on the reconstruction). In the following step, the physician gets the marked slices as a starting point to delineate the tumors, and can go up and down

the image stack to complete the delineation of each nodule. Different image processing features, such as filters and contrast enhancement controls are available that facilitate the identification of different tissues.

Regarding dosimetry analysis, the input data usually consist of a set of calculated doses for evenly spaced points on the anatomy. In the examples, these points are the centers of the  $1\text{ cm}^3$  cells that form the 3D voxel representation of the patient geometry, as obtained by NCTPlan. In order to determine the dose values for each point of the anatomy, and in particular on the surface, a trilinear interpolation is performed by SPHERE using the built-in capabilities of MATLaboratory. Then, SPHERE allows visualization of the 3D superficial dose distribution in the reconstructed anatomy, both for tumors and skin (Fig. 3). When the 3D reconstruction and a picture of the anatomy are registered, this gives a comprehensive overview of a treatment, since it allows visualizing dose distributions on skin and doses delivered to tumors. It is also possible to obtain the numerical dose value at any particular point of the anatomy surface. This has an important application: if a nodule is too small to appear in CT scans, the

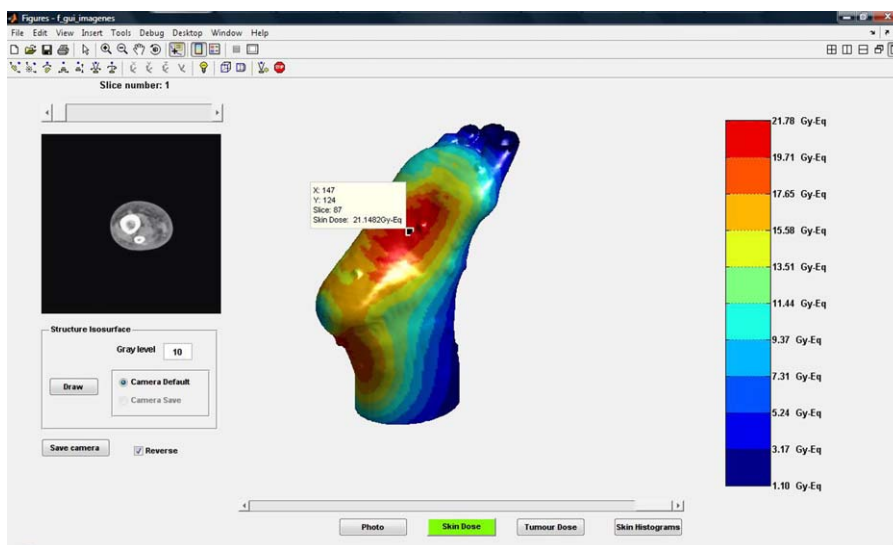


Fig. 3. Registration of the superficial dose distribution for normal skin and a picture of the patient anatomy.

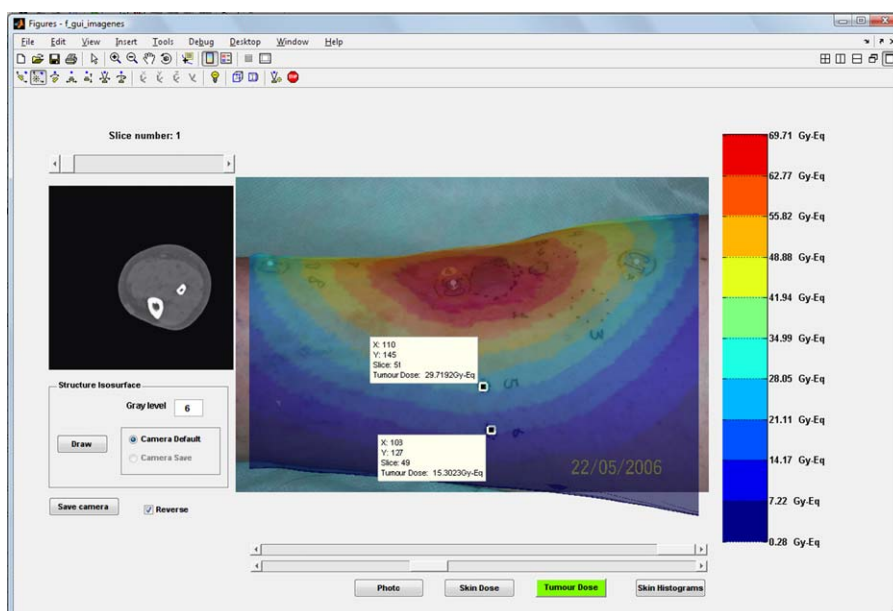


Fig. 4. Nodules 5 and 6 were too small to appear in TAC images. Dose values are obtained from the superposition.

physician can obtain, with the help of the anatomy picture, the point tumor dose. For tumors large enough for delineation, a more accurate and complete information is obtained by the generation of cumulative dose-volume histograms. Moreover, isodose curves can be superimposed to any TAC slice.

The tool also helps study skin dosimetry. Visual information is provided by the already mentioned 3D superficial dose distribution on the reconstructed anatomy. A more quantitative analysis can be performed by means of cumulative dose–area histograms. In order to generate these histograms, areas on the anatomy surface must be computed. This is done making use of the MATLAB internal routines for surface generation.

The clinical case in Fig. 4 represents several lesions of different sizes. For example, nodule 1 is large enough to appear in TAC images. However, nodules 5 and 6 are of small size, and could not be delineated. The figure shows how the doses delivered to those nodules are computed and reported by the program.

### 3. Results

The new computational tool made it possible to complete the tumor dosimetry of the Argentine treatments of cutaneous nodular melanoma, since it allowed to deal with lesions that were difficult or impossible to identify in medical images with the previous available capabilities. It also helped performing the tumor delineation of the last clinical trials carried out in Argentina. The completion of the tumor dosimetry allowed an extended investigation of the possible influence of tumor size and total dose on the local tumor response and to establish preliminary values of control doses for tumors in some volume range (González et al., 2009). It is worth noticing that the visualization of the 3D dosimetry can be also helpful in the treatment planning process. It provides a simple way to assess a treatment and compare different candidate plans. Skin areas with doses around tolerable limits or tumors with low doses become apparent in the visual dosimetry distribution.

A thorough description of skin dose distributions of all melanoma treatments performed with BNCT in Argentina was obtained. Cumulative dose–area histograms were generated and a set of dose-based figures of merit for skin were calculated. These figures of merit were contrasted to observed skin toxicities, in order to initiate an analysis of their possible correlation (González et al., 2009). The long term objective is to find a good predictor of skin toxicity based on dose distributions to optimize the prescription process. An accurate representation of the dose distribution in the skin is also of central importance in dynamic infrared imaging (DIRI) research applied to BNCT of melanoma (Santa Cruz et al., 2009). A preliminary study based on a patient treated with BNCT and studied by means of DIRI showed consistency between the acute skin reaction, the temperature distribution and the superficial skin dose distribution.

#### 4. Conclusions

The present work was carried out in the context of the Argentine project of BNCT treatments for cutaneous melanomas. Thus, the quantification and analysis of the dosimetry in the normal skin has been one of the main concerns. The capabilities developed to this end could be useful to other BNCT applications for which skin is considered an organ at risk.

All the features of the SPHERE proved useful for retrospective dosimetry analysis and have potential use at the treatment planning stage.

#### References

- González, S.J., Santa Cruz, G.A., Kiger III, W.S., Goorley, J.T., Palmer, M.R., Busse, P.M., Zamenhof, R.G., 2002. NCTPlan, the New PC version of MacNCTPlan: improvements and verification of a BNCT treatment planning system. In: Sauerwein, W., Moss, R., Wittig, A. (Eds.), Proceedings of the Tenth International Congress on Neutron Capture Therapy. Monduzzi Editore, Bologna, pp. 557–561.
- González, S.J., Bonomi, M.R., Santa Cruz, G.A., Blaumann, H.R., Calzetta Larrieu, O.A., Menéndez, P., Jiménez Rebagliati, R., Longhino, J., Feld, D.B., Dagrosa, M.A., Argerich, C., Castiglia, S.G., Batistoni, D.A., Liberman, S.J., Roth, B.M.C., 2004. First BNCT treatment of a skin melanoma in Argentina: dosimetric analysis and clinical outcome. *Appl. Radiat. Isotopes* 61, 1101–1105.
- González, S.J., Carando, D.G., Santa Cruz, G.A., Zamenhof, R.G., 2005. Voxel model in BNCT treatment planning: performance analysis and improvements. *Phys. Med. Biol.* 50, 441–458.
- González, S.J., Casal, M., Pereira, M.D., Santa Cruz, G.A., Carando, D.G., Blaumann, H., Bonomi, M., Calzetta Larrieu, O., Feld, D., Fernández, C., Gossio, S., Jiménez Rebagliati, R., Kessler, J., Longhino, J., Menéndez, P., Nieves, S., Roth, B.M.C., Liberman, S.J., 2009. Tumor control and normal tissue complications in BNCT treatment of nodular melanoma: A search for predictive quantities. *Appl. Radiat. Isotopes*, this issue, doi:10.1016/j.apradiso.2009.03.038.
- Menéndez, P.R., Roth, B.M.C., González, S.J., Santa Cruz, G.A., Blaumann, H., Calzetta Larrieu, O.A., Feld, D.B., Casal, M.R., Jiménez Rebagliati, R., Nieves, S.I., Longhino, J., Pereira, M.D., Fernandez, C., Kessler, J., Liberman, S.J., 2009. BNCT for skin melanoma in extremities: Updated Argentine clinical results. *Appl. Radiat. Isotopes*, this issue, doi:10.1016/j.apradiso.2009.03.020.
- Santa Cruz, G.A., Bertotti, J., Marín, J., González, S.J., Gossio, S., Alvarez, D., Roth, B.M.C., Menéndez, P., Pereira, M.D., Albero, M., Cubau, L., Orellano, P., Liberman, S.J., 2009. Dynamic infrared imaging of cutaneous melanoma and normal skin in patients treated by BNCT. *Appl. Radiat. Isotopes*, this issue, doi:10.1016/j.apradiso.2009.03.093.