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Feasibility of 3D printing for customized radiotherapeutic models to be used in superficial skin cancer therapy

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Abstract: Skin brachytherapy is an effective treatment for patients with skin cancers. It is based upon the use of an applicator containing a gamma-emitting source located near the tumor. For superficial and shallow skin tumors close to sensitive structures, we propose a new brachytherapy method using 3D printing technology employing beta-emitting isotopes. The beta-emitting patches would allow for directed, effective and controlled dose delivery to the skin tumors, thus mitigating exposure to sensitive structures.

I. Introduction

Radionuclide brachytherapy is an effective method for treating skin tumors [1]. In this technique, a gamma-emitting isotope shielded within an applicator is placed upon the skin's surface to irradiate the lesion. For small tumors located on flat surfaces, the applicator is a cup-shaped shielding with a circular opening of 10-, 20- or 30-mm diameter to direct the radiation dose [1]. Although one can choose the applicator based on the size of the tumor, it is not possible to shape the radiation dose to the tumor outline. In the case of larger tumors or those located in areas with curved anatomies, a flexible, catheter-based mesh applicator tunneled inside silicon spheres is used [1]. Due to the flexibility of this applicator, it can contour to the curved anatomy of the affected area. However, exact conforming of the radiation dose based on the 2D shape of the tumor on the skin surface is not possible.

Due to the inherent toxicity of ionizing radiation, it is of critical importance to deliver the maximum dose to the tumor volume while minimizing radiation exposure of the surrounding healthy tissue. In cases where the skin tumor is very close to a critical organ, such as the eye or right on top of a sensitive structure such as bone, protection is critically important.

In the current work, we are presenting an approach to 3D print customized radiotherapeutic patches for brachytherapy of superficial skin tumors. The digital model for printing the patches is based on the specific tumor information obtained pre-treatment using imaging modalities such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT). This information includes the 2D shape and size of the tumor on the skin's surface as well as the depth information. With that, a printed model could be created that provides a therapeutic solution with an individualized dose profile. Once this printed patch is placed over the tumor surface, the radiation beam in the entry of skin will be confined mainly to the tumor surface anatomy and the treatment depth matched to the tumor extension through the applied radiation source.

The radioactive model is fabricated through extrusion and solidification of a hydrogel, which is mixed with a clinical beta-emitting radioisotope such as Yttrium-90 (Y^{90}) or Holmium-166 (Hol^{166}). Beta particles are energetic electrons that have a sharp dose falloff with a short range in tissue, usually less than 10 mm [2]. With that, they deliver a significant part of their energy within a few millimeters of the tissue. This characteristic makes beta-emitters impractical as universal brachytherapy sources for all types of skin tumors. However, it could be a feasible option for treating shallow superficial skin tumors, especially those located close to radiation-sensitive structures [3-5]. Also, dose shaping of beta particles is easier to achieve compared to gamma radiation.

The isotopes used to mix with the extruded material of the 3D printer can be either radioactive or potentially-radioactive. In the latter case, the printed model containing the isotope is not radioactive but becomes radioactive after activation in a reactor.

The first prerequisite in 3D printing of radiotherapeutic patches is to obtain a uniform distribution of the isotope or isotope base material. By ensuring a uniform radiation dose in the length of the printed line it is possible to create the desired radiation dose profile by adjusting the digital model of the scaffold. Therefore, when the digital model is created based on the contour of the skin tumor, the radiation dose of the patch will match the surface anatomy of the skin tumor.

3D printing also would allow the fabrication of radioactive patches with an intensity modulated dose pattern. This is achieved by printing specific parts of the

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patch with more than one line. The desired dose pattern is obtained only if the extruded lines contain isotopes with a uniform distribution pattern.

The aim of this work was to print a 3D model with a hydrogel containing an added isotope and to verify its distribution within the printed lines.

II. Material and methods

As a proof-of-concept, we used a starch-based colloidal system containing magnesium and 3D printed a lattice scaffold. Magnesium was used as a representative of any radioactive or potentially-radioactive isotopes that can be used for our project. Due to the non-radioactive nature of magnesium, we could perform our experiment in a standard laboratory.

In this study, the colloidal hydrogel was a mixture of magnesium chloride ($MgCl_2$) and starch. Briefly, a saturated $MgCl_2$ solution (~0.2M) was prepared. Next, research grade starch was gradually added at 80°C until completely dissolved.

To print the magnesium-containing colloid, an Aether 1 bioprinter (Aether, US) was used. We fitted a 20cc barrel with a 22G needle (inner diameter of 0.7 mm) and used it to print an orthogonal lattice pattern.

To verify the $Mg2^+$ distribution within the printed lines, we scanned the scaffold using a micro-CT scanner (Scanco, Switzerland). It was set at 12 µm voxel size, 45kV, 177 µA, and 300 ms exposure time. The image was then analyzed by ImageJ to produce line profile.

III. Results and discussion

3D printing of a 12 by 12 lattice scaffold of starch that contains magnesium particles and the micro-CT image of a four by four lattice scaffold printed with the same hydrogel is shown in Fig. 1. Red dash lines in the micro-CT image show the lines used for evaluation of particles distribution. Due to the high water content and compliant nature of the colloid upon printing, contraction and deformation was noted. Further optimization and functionalization of the base polymer is suggested to render the printed material more stable. Distribution of magnesium particles within the deposited starch is seen by its higher contrast in the image.

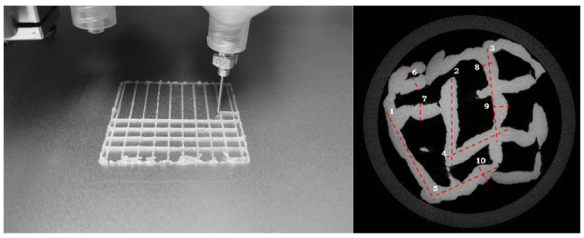

Figure 1 3D printing of a 12 by 12 lattice scaffold with starch containing magnesium (left image) and micro-CT image of a four by four scaffold of the same hydrogel

For the quantitative assessment of the particle distribution, line profiles in the length and width (5 each at different locations) of the printed lines of the scaffold were produced. The averaged gray values of the lines and their standard deviations were 140 to 165 and 8.09 to 9.98, respectively. The low variations of the gray values could be an indicator of the fairly uniform distribution of particles in the printed model.

We conclude that when the radioactive model is printed based upon the 2D shape of skin tumor, the dose profile will have a uniform distribution limited to the 2D shape of the tumor. To modulate the radiation intensity, parts of the scaffold can be printed with more than one layer of the extruded line to have a higher intensity of the radiation dose in that area. Alternatively, the scaffold can be printed using a multi-barrel 3D printer with hydrogels of different concentrations of the isotope.

It should be mentioned that the concept proposed here is based on beta-emitting isotopes. In comparison to the commonly used gamma radiation in skin brachytherapy practices, beta particles have a shorter range in tissue. Therefore, they are not suitable for treating thick skin lesions, which extended more than 3-4 mm in skin tissue. Beta radiation therapy of thicker lesions will lead to an undesirable increase in the skin surface dose. This is a potential constraint of our proposed idea which limits its application for superficial thin skin tumors.

IV. Conclusions

3D printing technology has the potential to fabricate individualized radiotherapeutic patches for use in superficial thin skin cancer therapy. As the subject for the future work, the experiment will be replicated with a beta-emitting isotope for better assessment of the dose distribution of the printed lines. Also, the mechanical property of the printed model is going to be optimized so that it can be used on the skin surface.

Author's statement

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