Integrating hyperthermia with wireless, bioresorbable, flexible, and implantable bioelectronic drug delivery device for brain tumors

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***Abstract*— A combined treatment using hyperthermia and wireless chemotherapy increases the effectiveness in treating brain cancer tissue. This paper reports an implantable, bioresorbable, biocompatible, and flexible bioelectronic patch, activated wirelessly to deliver the drugs to the tumor region. Cancer tissue is first treated using hyperthermia, a curative and noninvasive approach wherein an increase in temperature of 40-45℃ is required at the tumor location. The target temperature is achieved using an annular phased array of antennas, altering the phase and amplitude of individual antenna so that wave is constructively added at the tumor region and destructively added elsewhere. Once the target temperature is provided to the tumor for enough time, the beam of antennas is steered at the bioelectronic patch. Consequently, drug delivery to malignant tissue is started. After treatment, the bioelectronic patch degrades into the tissue. Hence, no post-surgery is required to remove the implanted bioelectronic device.**

***Index Terms*—Hyperthermia, Chemotherapy, Bioelectronic Patch (BEP), Phased Antenna Array.**

I. Introduction

COMPARED to the past, science and medical technology are now more developed, and they are diagnosing and curing many diseases. However, treatment issues related to cancer are not completely solved yet [1]. Majority of people are most likely to diagnosed with adrenocortical carcinoma (29/90, 32.2%) and neuroendocrine neoplasms (22/90, 24.4%). Most of adrenal tumors which the first of diagnosis rate are treated by surgery as much as possible. But brain tumors are difficult to perform surgery because there are many risk factors. So, many studies are being conducted to inject drugs into brain tumors.

Among them used a bioresorbable electronic patch (BEP), which is flexible, sticky, and biodegradable wireless electronic device integrated with a bifacially designed polymer drug reservoir [3]. We think that applying BEP like this paper, but our plans to completely treat the brain tumors by in two steps. First step is to use hyperthermia to apply magnetic thermal actuation to brain tumors. And second step is to use chemotherapy to kill remaining brain tumor cells.

II. Treatment Technique

A. Hyperthermia

Fig. 1 illustrates the proposed idea where implantable and bioresorbable drug delivery medical devices is integrated with hyperthermia for the treatment of brain tumor.

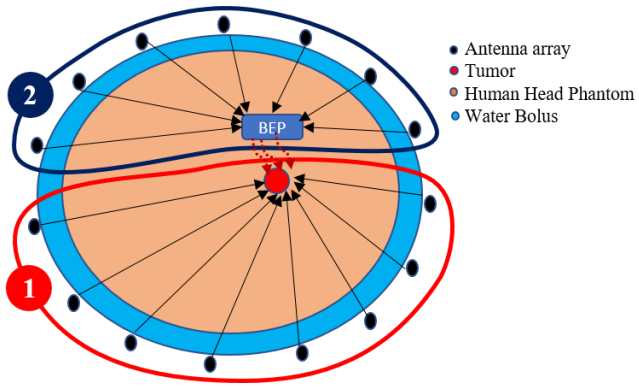
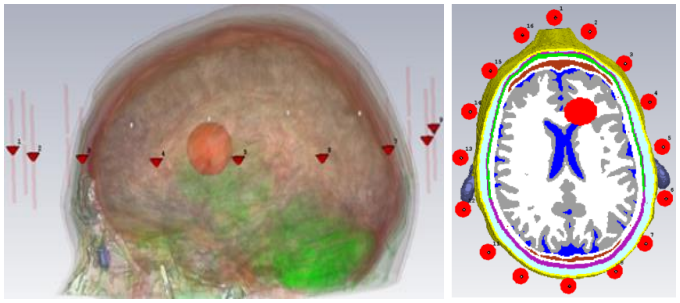


Fig. 1. Integrated hyperthermia treatment (red circle of 1) with wireless chemotherapy (blue circle of 2).

Implantable and bioresorbable drug-delivery medical devices for the treatment of various diseases have shown enormous reliability, safety, and efficiency [1]. The main advantage of these devices is that there is no need for post-surgery to remove the implanted device. Recently, the treatment of cancer tissues located in the brain using flexible, biodegradable, and wireless drug delivery devices were carried out [2]. In this article, bifacially designed hydrophobic devices were presented that helped in conformal adhesion on the brain surgery location and provided wirelessly controlled and thermally extended drug delivery to cancer tissue, whilst maintaining the nonintentional drug leakage to the surrounded normal brain tissues. Although the work presented in [2] showed good performance, further improvement in the quality of treatment is still necessary

To increase the efficacy of the implanted bioelectronic patch (BEP) loaded with a drug, instead of magnetic thermal actuation of the BEP, an annular phased array of antennas has been presented in this paper. This antenna array excluded the need for an implanted heater and that was integrated with BEP. The focused beam of the electric field elevates the required temperature around the temperature sensor, which in turn activates the drug delivery process. For the efficient treatment of the tumor region, hyperthermia (HT) is integrated with wireless chemotherapy. Hyperthermia is a curative and noninvasive technique that utilizes the electric field radiated from antennas to treat malignant cells. The electric field

penetrated the human head focuses only on the tumor region by changing the phase and amplitude of individual antennas. This subsequently, results in constructive interferences of waves at the target location which provides the desired temperature at the tumor area. Thereafter, the phase and amplitude of the antenna array varied to steer the beam of waves toward the BEP to activate the drug delivery system.



(a) (b)

Fig. 2. (a) Realistic head model surrounded by antenna array. (b) Top view of inner part.

B. Chemotherapy

Chemotherapy is a drug treatment that use chemical drugs to kill the cells in the body. Chemotherapy is most often used to treat cancer. The BEP, which is used in previous work, together with an associated mild-thermic actuation protocol, provide spatially-controlled and temporarily-extended drug delivery to brain tumor [3]. Magnesium-based ultra-thin electronic devices, which work as a wireless heater for mild-thermic drug delivery actuation and a wireless temperature sensor for controlled mild-thermic actuation, are embedded in thin films.

In this paper, a more compact implanted wireless heater BEP is proposed by eliminating wireless heater for mild-thermic drug delivery actuation. In order to replace the implanted wireless heater, we propose another heating system that use the Phased Array External Antenna. The electric field applied by an external antenna triggers heating in the implanted BEP, resulting in the increased temperature of the BEP and surrounding brain tissue. The amount of the drug release can be controlled by mild-thermic actuation. So we can optimize the amount of drug release by controlling the instrumental parameters such as the RF frequency, coil-to-BEP distance, etc. The appropriate level of mild-thermic actuation promotes the drug release.

III. EXPECTED RESULTS

The first step of hyperthermia can treat almost all tumor cells because it focuses electric fields on brain tumors with antennas to induce heat of the cells themselves. In addition, since the focus position of the electric field can be adjusted, the heating effect can be the same regardless of the location of the tumor. Since there may be small but remaining tumors after hyperthermia treatments, the second step, chemotherapy is used. Chemotherapy can control the applied heat and inject the right amount of drug depending on the amount of remaining tumors to increase the cure rate more effectively. This two-step treatment method will be faster and more effective than using only one method to complete recovery the brain tumors.

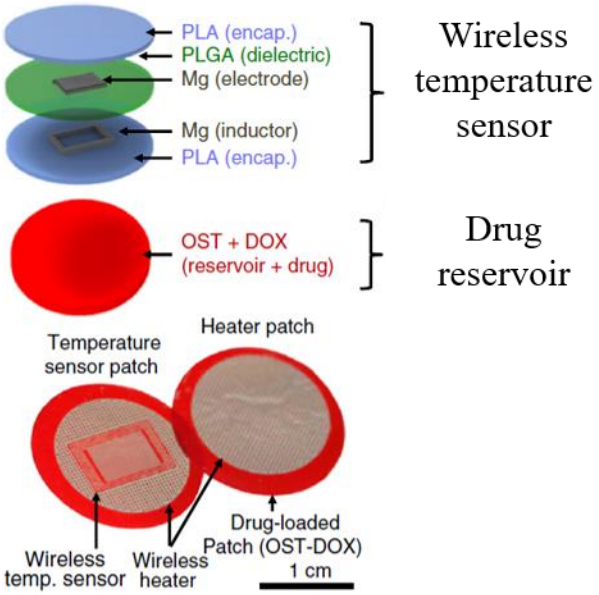


Fig. 3. Expected structure of bioresorbable electronic patch (BEP) without heater.

IV. CONCLUSION

In treatment, BEP, a bioresorbable, implantable, flexible material, is used to reduce the effects of toxins, and it can maintain lightness while having strength that does not easily break in vivo. Also, it has the advantage of being convenient to do wireless heating because it can be processed in compact patch form. The uniqueness of this idea is that wirelessly apply electric field to the tumor cells and BEP at any given intensity. Therefore, doctors can establish specific treatment schedule based on patients' individual recovery conditions. In addition, this method idea is no need of post surgery because of using bioresorbable material, so it can minimize invasive methods such as surgery or drug treatment using injections. And maybe it can applied not only to the brain but also to other organs.

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