An optical-telecommunications-based technique to disrupt stroke using the artery as an acoustic Biological fiber

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Abstract

Because the number of applications for therapeutic and diagnostic medical ultrasonound systems continue to increase, there is a need to improve the efficiency of these acoustic techniques. In this frame, this paper reports on a new mildly invasive therapeutic method to disrupt stroke. The proposed method is based on the propagation of ultrasound waves inside a carotid artery, which is viewed as an optical fiber. The challenge, then, is to determine the feasability and the efficiency of such technique. The preliminary results of this study are presented. At 1 MHz ultrasound frequency, the penetration depth is about 21.7 cm, which is sufficient to reach and dissolve cerebral clots by transmitting an incident wave relatively far from thrombosis location. To reach this penetration depth, a saturation acoustic pressure of 1.5 MPa must be not exceeded. A temperature rise rate of about 0.46 °C/s for an intensity of 100 W cm^{-2} is observed. Pulsed waves are used to enhance cavitation, which is considered as the most likely and dominant mechanism for blood clots disruption. The project is embedded in the framework of a collaboration project involving three Canadian universities namely, Université de Sherbrooke, Université de Québec à Montréal and Université de Moncton.

Sommaire

Puisque l'utilisation des ultrasons pour des applications thérapeutiques et diagnostiques continue à augmenter, il y a un besoin d'améliorer l'efficacité de ces techniques acoustiques. Dans ce cadre, cet article traite une nouvelle méthode thérapeutique modérément invasive pour le traitement des maladies thrombotiques cérébrales. La méthode proposée est basée sur la propagation des ondes ultrasonores dans l'artère carotide, qui est regardée comme étant une fibre optique. Le défi, alors, est de déterminer la faisabilité et l'efficacité d'une telle technique. Les résultats préliminaires de cette étude sont présentés. À une fréquence d'ultrasons de 1MHz, la profondeur de pénétration est environ 21.7 cm, qui est suffisant pour atteindre et dissoudre les caillots cérébraux en transmettant une onde incidente relativement loin de la thrombose. Pour atteindre cette profondeur de pénétration, une pression acoustique de saturation de 1.5 MPa ne doit pas être excédée. On observe un taux d'élévation de la température d'environ 0.46 °C/s pour une intensité de 100 W cm^{-2}. Des ondes pulsées sont employées pour favoriser la cavitation, qui est considérée comme le mécanisme le plus susceptible et dominant pour la destruction des caillots de sang. Le projet entre dans le cadre d'un projet de collaboration entre trois universités canadiennes notamment, l'université de Sherbrooke, l'université de Québec à Montréal et l'université de Moncton.

1.0 Introduction

Thrombosis is the presence of a coagulated blood clot inside a blood vessel causing a deceleration of the blood flow (Figure 1). When the clot is located in the brain, it may cause a stroke, also called a brain attack (Figure 2). It is well known that this cardiovascular disease represents an important cause of death in the world. The main treatment of stroke is medicines and drug therapy which will thin the blood and make it flow more easily. Furthermore, surgery can be employed to treat acute stroke or to repair vascular damage in the brain [1]. Meanwhile, therapeutic methods based on the application of ultrasound waves have also been used to disrupt strokes in vivo and in vitro. However, there is currently an additional interest in this problem due to progress in bioacoustics.

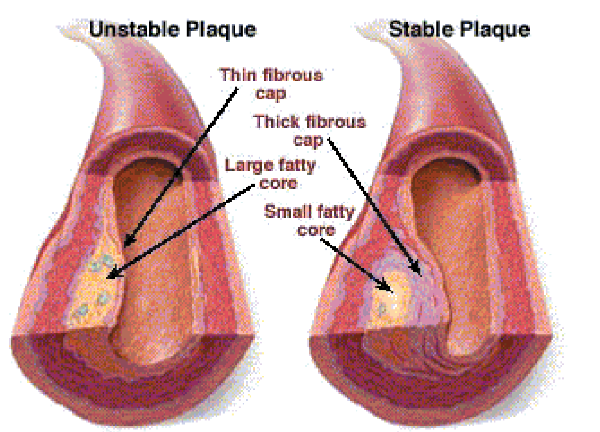

Figure 1: Plaque blocking the artery

It is well known that the ultrasound is widely used in medical diagnosis and therapy. On the one hand, the ultrasound energy is a non ionizing radiation, which does not impose hazards such as chromosome breakage and cancer development. On the other hand, it has several physiological effects based on the increase of inflammatory response, on the repair of the damaged tissues and on the heating of soft tissues.

A number of medical applications such as the ultrasound therapy of the occlusion of blood vessels were proposed. The methods based on the application of ultrasound waves use either an ultrasonic energy guided by a catheter [2], or an ultrasound radiation [3]. The first method has been used to dissolve clots in vitro, in animal models and in patients [2], whereas the second method has been reported in vitro and in animal models [3].

Both techniques have engineering problems. Most of the technical disadvantages of a catheter system are due to its poor efficiency as a RF/W radiation source. Consequently, the power loss in the coaxial cable and its subsequent heating during power delivery lead to a breakdown in the dielectric and the catheter material. In addition, there is the difficulty of designing a unidirectional antenna that can radiate energy into the diseased and not the surrounding healthy tissues. These limitations are unacceptable when a catheter system is used to treat life-threatening venous disorders, stable and unstable plaque, arteriosclerosis, or deep-seated tumor. The technical problems related to the radiated waves take on a different form and concern both diagnostic and therapeutic aspects related to physics and to the engineering of hyperthermia. With this technique, the incident wave undergoes multiple scattering inside the patient's body and, because the evanescent waves are difficult to mea-

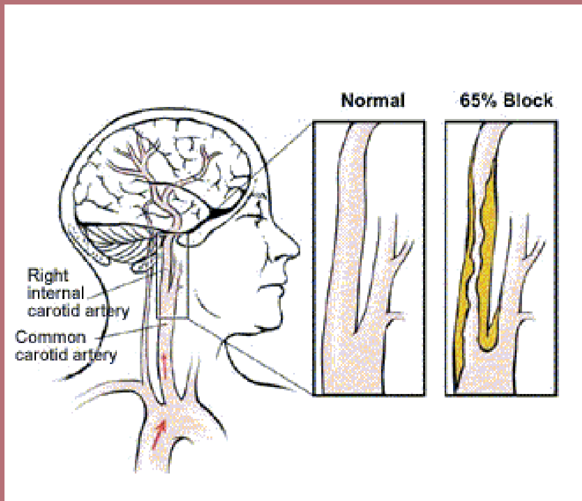

Figure 2: Artery hardening

sure, high spatial-frequency informations are mostly lost. Moreover, negative hyperthermal effects are associated with the exposure to external ultrasound energy [4].

To overcome many limitations of these ultrasound therapeutic methods, a new approach inspired from optical telecommunications has been recently advanced. The technique is based on propagating a pulsed ultrasound waves through the artery like light propagating through a single mode fiber. Cavitation effects near the solid boundary of the waveguide, namely the artery, are created to destruct the undesired obstacle. This quasi non-invasive ultrasound therapy for clots and strokes disruption has been proposed and investigated in the framework of a collaboration project involving three Canadian universities namely, Université de Sherbrooke, Université de Québec à Montréal and Université de Moncton.

In this paper, the new approach, inspired from fiber telecommunications, and the associated phenomena will be summarily described. Then, the relevant parameters related to this technique will be shown. Last, some interpretations and conclusions will be drawn based on recent results, and future prospects are considered.

2.0 From the optical fiber to the artery

Interest has grown in recent years in the use of ultrasound propagation as a therapeutic mean to treat the vascular disorders. The different therapeutic applications of ultrasound like stone destruction, cells ablation by cavitation and tissue heating by acoustic absorption, are the foundation of several medical applications. The power of ultrasound waves lies on their ability to reach deeply situated tissues using either in a non-invasive or an invasive method.

Essentially, the idea stems from the fact that an acoustic wave can propagate either as a radiated wave or as a guided wave, like light propagation inside the optical fiber. To guide a wave, either a transmission line or a waveguide must be used. In the problem at hand, where we want to get rid of some kind of obstruction within an artery, the transmission line approach did not quite solve the problem (see the previous discussion on catheter systems). The technique that we propose to study takes on the perspective that an artery can be considered as a dielectric circular waveguide like the optical fiber (Figure 3). Furthermore, to achieve a deep penetration sufficient to reach the defective location (sufficiently large skin depth) while maintaining the injected acoustic power, single mode propagation is desired like in the case of optical light transmission through the optical fiber. We remind the reader that one of the main advantages of the single mode optical fiber is its inherent low attenuation during propagation which leads to longer cable runs between repeaters, without forgetting its remarkably and excellent linearity and dispersion behavior.

Any ultrasonic field can create a mechanical disturbance in the propagation medium, namely the artery. The resulting changes of pressure, tension, shear stress, expansion, compression, velocity and acceleration can all have an impact on the biological system. In an absorbing and dissipative medium, part or all of the mechanical energy is converted to heat. Another important effect is cavitation, with the generation of local micro-currents associated to the presence of microbubbles in the medium [4].

To the best of our knowledge such a general model does not exist yet, and its formulation is beyond the scope of the review article presented here. The question therefore is: can an artery work as a waveguide (like the optical fiber) that can propagate energy until the location of the obstruction in order to dissolve it, by heating and/or by shaking using an acoustic wave? The artery including the obstacle becomes, with regard to the wave, a lossy waveguide (a fiber with attenuation). For our purpose, one of the carotid arteries is used as an ultrasonic biological fiber (Figure 4).

3.0 Model description

3.1 Physical properties of the carotid

The main arteries that supply blood to the brain are the two common carotids. They both originate from the arch of the aorta (via the brachiocephalic artery for the right common carotid), and each of them bifurcates at the level of the upper border of the thyroid cartilage into an internal and an external carotid artery. The internal carotid ascends to enter the skull via the carotid canal to the middle cranial Fossa. The external carotid, which begins opposite the upper border of the thyroid cartilage, has many branches along its course up the neck and supplies the neck and face [5]. Earlier studies have shown that the normal human carotid diameter varies between 3 mm and 5 mm [6] and its wall thickness is about 0.5 mm [7]. This results in an average interior carotid radius of 1.5 mm. The most common cause of a stroke is in general due to the development of clots in the carotid arteries. This may be the consequence of a thickening and/or hardening of the artery walls [5].

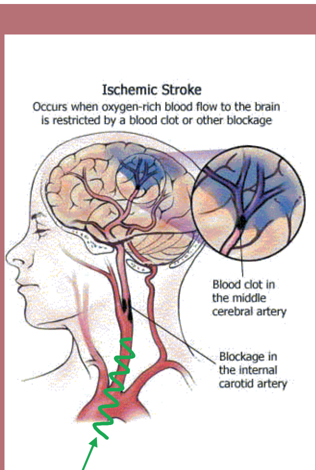

Figure 3: Injection of ultrasound wave in the carotid

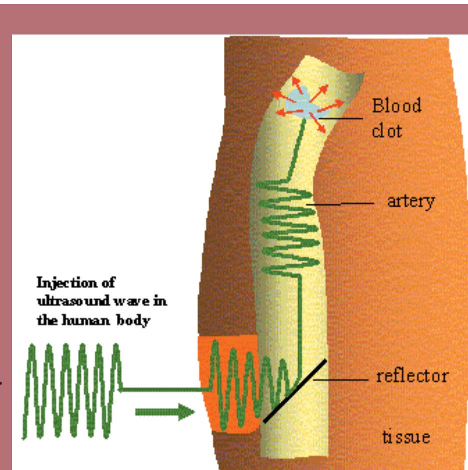

Figure 4: A model of ultrasound wave propagation in the artery

3.2 Physiological effects of ultrasound energy and the choice of the adequate mode

The study of acoustic properties of tissues and the investigation of the effects of ultrasound on biological cells have received attention in the last few decades because of its important role in therapeutic applications. Physically, because tissues are absorbent, they warm up during the travel of the ultrasonic field inside them. Generally, the ultrasonic field is not uniform and the absorption coefficient of tissues varies from one point to another.

Temperature rises by increasing the kinetic energy of tissue molecules, which is then converted into heat, and by increasing the production of unstable cavitation that occurs when the bubbles collapse violently under the pressure due to excessive energy accumulation, once a critical size is exceeded. A large, brief, local pressure and temperature increase are the results of this implosion. Moreover, the reflection of the ultrasounds on the dense structures also causes a significant temperature increase in the tissue/obstacle interface.

Besides, the enzymatic activity within the body doubles for each increase of 10°C. If the temperature becomes higher than 45°C, the enzymes are denatured, so that their activity is initially decreased and then stopped. This has a significant impact on the cellular structure and its metabolism. Two different therapeutic ultrasound modes are typically used, namely pulsed non-thermal and continuous thermal ultrasound therapy.

A pulsed ultrasound wave produces a mechanical pressure during its travel through soft tissues. As a result, microscopic bubbles are generated in living tissues, the intra-cells are activated and the cell membrane is deformed. This phenomenon of cell membrane distortion is divided into three mechanisms [4].

The first one is the acoustic streaming that can be described by the radiation force or deformation of the tissue molecules (cell membrane) due to the compression phase of an ultrasound wave. The second mechanism is bubble formation, which is affected by the radiation force in the tissue fluids. The bubbles expand and contract under the effect of the radiation force (compression and rarefaction), adding further stress to the cell boundaries. Bubble expansion and contraction without growing to a critical size is referred to as stable cavitation. The last mechanism is microstreaming, which is a microscopic fluid movement, described by the phenomenon of cavitation.

The cavitation effect depends on the pulsed ultrasound properties such as low-intensity, high frequency, which limit the bubble growth. The lifespan of the cavities is short and is only determined by the frequency of the ultrasound wave. Cavitation decreases in reverse proportion to frequency increase. As a result, it requires more power to occur as frequency increases [3].

Our approach for stroke disruption is mainly based on acoustic cavitation [4], the phenomenon of nucleation, growth and collapse of vibrating microscopic bubbles when ultrasound waves pass through a liquid. A mechanical shock due to the oscillation of the microbubbles and their rapid collapse due to pressure effects may be felt up to a few radial distances from the collapsed cavitation [4].

In the immediate vicinity of the collapsing bubble, an intense shear stress may occur, especially in solids, which can change the erythrocyte membrane, break fibrin bonds, affect platelets and finally lead to stroke disruption [3]. This phenomenon is more effective when a gas bubble is close to a solid boundary (coagulated blood or other obstacle). An acoustic micro-current is generated meadows of the bubbles causing a great collapse, which can dissolve the clots.

4.0 Heat propagation

A thermal effect is also generated during the propagation of ultrasounds in the arteries. For solving the governing heat partial differential equation (PDE) the Laplace transform and the Fourier method were used. According to our numerical results shown in Figure 5, the temperature rise rate in blood and clot are: $(dT/dt)_{blood}=0.00095$ °C/s and $(dT/dt)_{clot}=0.00015$ °C/s.

5.0 Discussion

The focus of this presentation was to describe a new ultrasound therapeutic technique for the treatment of stroke. The main finding of the study was the study of the applicability of a new ultrasound therapeutic approach based on the modeling of an artery as a dielectric cylindrical waveguide, like the optical fiber. An acoustic wave propagates through this biological fibre, attains the obstacle and disrupts it by means of cavitation.

A growing number of laboratory and theoretical studies on bioacoustics suggest that the ultrasound application time depending on the frequency, the intensity and the rate of temperature rise must be respected. As the ultrasound frequency increases, more energy is lost and more power is required to produce cavitation. As a consequent, the heat deposition per unit volume increases causing therefore an overheating during a shorter time. All these parameters must be adjusted to avoid cell destruction [8].

A preliminary investigation shows that the use of arteries as dielectric circular waveguides (optical fiber) may lead to a potential thrombolytic therapy without incurring the limitations of the non-invasive therapeutic method based on the ultrasound radiation and the invasive ultrasound technique using the catheter [9].

Following this preliminary stage, we intend to carry out clinical and medical tests in vitro, on animal models and finally on patients.

6.0 References

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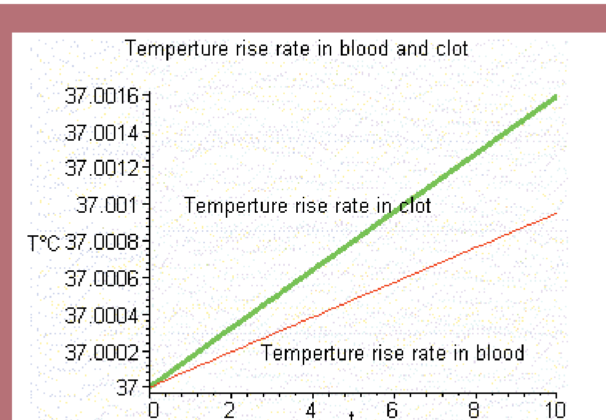

Figure 5: Temperature rise rate in blood and clot.

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