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**HYPERTHERMIA GENERATED WITH ARRAY OF
INTERSTITIAL ULTRASOUND WAVEGUIDE APPLICATORS**

by Doru Kaytar, Diploma Physicist

A thesis submitted to the Faculty of Graduate Studies and Research
in partial fulfilment of the requirements for the degree of

Master of Science

Carleton University, Ottawa, Ontario

April 1995

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**HYPERTHERMIA GENERATED WITH ARRAY OF
INTERSTITIAL ULTRASOUND WAVEGUIDE APPLICATORS**

submitted by Doru Kaytar, Diploma Physicist, University of Bucharest, Romania
in partial fulfilment of the requirements for
the degree of Master of Science

Thesis Supervisor

Chair, Department of Physics

Carleton University

ABSTRACT

Beside radio- and chemotherapy which are well established cancer treatment modalities, hyperthermia has relatively recently emerged as another method. This thesis presents and evaluates an original system to produce localized hyperthermia. The system uses an array of interstitial ultrasound waveguide applicators to deliver ultrasound energy to the volume of interest where this energy is converted into heat. Ultrasound, at frequencies around 1 MHz, is produced by a 12.7 mm diameter piezoelectric disk generating longitudinal waves. The applicator uses 1.1 mm diameter hypodermic needle as the waveguide of surface modes. The surface modes deposit their energy into the medium from the unclad part of the waveguide. It has been found that the heating efficiency depended in the first place on the waveguide radius that defines the divergence of the radiated beam. Attenuation has been less important, with the effects of absorption within the medium vanishing at radial distances larger than 1 cm. For applicators operated at 30 V rms, cladding of the waveguide has resulted in about 10% decrease of the energy output. With up to four applicators, hyperthermic temperature elevation of about 6°C has been produced in as large as 240 cm³ tissue phantoms of high thermal conductivity. Hyperthermia simulations using Finite Element Analysis showed uniform temperature elevations of at least 6°C in the region enclosed by the array. The average difference between experimental and simulated temperatures at ten locations was 0.0°C, with a standard deviation of $\pm 0.5^\circ\text{C}$.

REMARKS AND ACKNOWLEDGEMENTS

You'll see in this thesis not very much of hundreds of hours of polishing rings, cleaning contact surfaces, soldering tiny wires, drilling plastic containers and winding small solenoids. Everything would have been much more difficult without the continuous technical help and suggestions of Jim Sliwka. All that work has been hidden into colours, to avoid cumbersome symbols on the same graph, or to suggest the third dimension.

Units have been used appropriately for IUWAs experimental conditions. Power has been expressed in Watts, temperature in °C, but for distances I oscillated between cm or mm. Same with the mass expressed in grams, although in some cases for density I used kg. In all estimations and simulations, units were used in a consistent manner.

Experimental results presented here were possible only by the generous help I received concerning the instrumentation. I want to thank to Ernie Neuheimer from CRPP, Art Thansadote from Health Canada and John Rushby from our department for lending me some precious equipment. Also I want to thank everybody from the Physics Department, for advising me and for the logistic support I have got during my thesis.

Much of this study was based on the financial support arranged by Dr. Vasco da Silva from Ottawa Civic Hospital. I want to thank him for giving me this opportunity.

I must confess I was uneasy to use the subject 'I' for any of the sentences which will follow. All you'll read from here on was the common effort of Dr.B.J.Jarosz and myself. It was the result of a non-stop, bi-directional exchange between him and me: of data, hypothesis and especially intuitions, which constitutes the meat of any experimental research. I want to dedicate this thesis to B.J.J, who let me think free.

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1. INTRODUCTION

1.1 Hyperthermia therapy

When mammalian cells are exposed to temperatures above normal, they lose their reproductive capabilities. The loss of these capabilities, expressed by the decrease in surviving fraction, is demonstrated in fig.1 for CHO cells exposed to temperatures below and above 43°C. The surviving fraction depends on the interval of time cells were exposed to heat, and the hyperthermic (from greek: hyper = in excess, therma = temperature) conditions.

Figure 1: mammalian cell heat response, below and above 43°C [10]

Accepted normal temperature of the human body is 37°C, while hyperthermia is considered to be any temperature at and above 40°C [11, p.8]. *In vitro* cell damage was noted around 41°C if temperature was maintained for sufficiently long times [11, p.12-13]. At higher temperatures (up to 46°C, where protein coagulation can occur quickly), exposure times become shorter (for values, see tables 2.3 and 2.4 in [11]). In the present study, experimental temperature elevations in excess of 5°C were targeted. Also, the 5°C

was considered as the lower value for the simulated hyperthermic fields.

Presently there is a general trend to consider hyperthermia as complementary to other treatment modalities. Considered as a sensitizer, even smaller temperature increase would enhance the radiation effects. The degree of thermo-radiosensitization for low-dose-rate irradiation at 39°C, 40°C and 41°C was recently investigated [31]. The oncogenic potential of hyperthermia combined with radiation is discussed in [38], and encouraging results of hyperthermia combined with chemotherapy are presented in [40].

This project has originated from a clinical need to expand the heating range of the interstitial ultrasonic waveguide applicator (IUWA). The IUWA has been originally conceived in this department ([1] - [4]). In this study, a theoretical explanation of the acoustic waves produced by this device is proposed. An analysis of the applicator output for different designs is given. In order to increase the heating volume, an array of four such applicators has been designed and studied. Theoretical possibilities and limitations of the array are compared with the experimental results. Further directions to increase the device performances are suggested.

1.2 Hyperthermia techniques

Heat can be delivered to the tissue either by using an external applicator or invasively by an interstitial one [12]. The process of heat delivery can be purely conductive (as in the ferromagnetic seeds approach [41]), or by using electromagnetic (EM) or ultrasonic (US) heat sources. Recently, EM techniques have been discussed in [42], [43]. The wave propagation velocity v is $\sim 10^8$ m/s for EM, but only $\sim 10^3 - 10^4$ m/s for US sources. As for both fields there is:

$$\lambda = \frac{v}{f} \quad (1)$$

a trade-off between the wavelength (related to the source size), λ , and frequency, f , takes place. In the EM case, the high velocity requires a high frequency to get a reasonable source size (e.g. microwaves), or large source sizes to be operated at low frequencies. In the case of external sources, lower frequencies are also desirable because for the plane waves the deeper heating occurs at lower frequency ([12], p.91).

The US propagation velocity allows the wavelength (and the corresponding piezoelectric thicknesses) to vary from a fraction of a mm up. For external methods, the US heating limitations are the interface effects (tissue/air or tissue/bone boundaries) because of their different acoustic impedances. The present interstitial heating method is intended for deep seated brain tumours and it circumvents the above interface effects.

1.3 Interstitial US hyperthermia techniques

Beside the present array of four US waveguide applicators (both systems were recently presented in [37]), the only other known interstitial US device has been proposed by K.Hynynen and C.J.Diederich ([26], [27], [39]). Their applicator, presented in fig.2, consisted of several PZT cylinders radiating waves directly within the tumour and will be referred to in the following as the cylindrical piezoelectric transducer (CPT). Temperature elevations up to 9°C in liver *in vitro* have been reported for an array of four applicators operated at 9.5 MHz. Each of the applicators had 1 mm outer diameter, they were 2.5 cm long and they were located at the corners of a 14 mm square.

There are several basic differences between the two applicator systems:

Figure 2: Interstitial cylindrical piezoelectric transducer of Hynynen and Diederich [27]
a) piezoelectric applicator b) experimental set-up

- wave generation: for the CPT, waves were generated directly within the medium by piezoelectric oscillations in the thickness mode; in the case of IUWA the acoustic transformer converts longitudinal waves from the piezoelectric into surface wave modes: these propagate along the waveguide and the exposed end of the waveguide deposits this energy into the medium.

- operating frequency: around 9.5 MHz for CPT and 1 MHz for IUWA. For CPT, the piezoelectric wall thickness puts constraints on the frequency used. The piezoelectric disk of IUWA can be of any thickness, leaving a free choice for frequency.

- different designs: additional cooling of the piezoelectric required for CPT; the IUWA piezoelectric location, external to the heated volume, allows a very simple design.

2.INTERSTITIAL ULTRASONIC WAVEGUIDE APPLICATORS

A cross-section diagram of a single interstitial ultrasonic waveguide applicator (IUWA) is given in fig.3. The figure shows the main components of the applicator. Several designs have been used for the acoustic transformer and they will be described later. Fig.4 presents details of the transducer casing, while fig.5 specifies the cylindrical coordinates for the applicator's antenna.

In order to get the best ultrasound power output from each of the array's applicators, a considerable effort has been made to redesign, analyze and improve each of the applicators components. The cylindrical aluminium casing (1) in fig.4 holds everything together. It provides the ground to the piezoelectric and plays a role in cooling the piezoelectric. The coaxial cable (2) has the ground going to a pin (2') at the casing, while the signal goes to the metallic side of the contact ring (3). In order to have the ring in continuous contact with the piezoelectric during vibration, a compressional spring (4) has been provided of appropriate spring constant.

Figure 3: Main components of IUWA

Figure 4: Details of transducer casing

Figure 5: Coordinate system used

Acoustic energy is provided by the APC-850 PZT piezoelectric ceramic (5). It oscillates in the thickness mode at around 1 MHz. Some of the piezoelectric characteristics reproduced from the technical data sheet are presented below:

Table 1 Piezoelectric APC-850 characteristics:

thickness = $2.03 \text{ mm} \pm 0.05 \text{ mm}$
 diameter = $12.7 \text{ mm} \pm .4 \text{ mm}$
 frequency = 1 MHz
 density = 7.5 g/cm^3
 longitudinal coupling coefficient $k_{33} = 72 \%$
 longitudinal deformation coefficient $d_{33} = .0005 \text{ } \mu\text{m/V}$
 Curie temperature = $360 \text{ } ^\circ\text{C}$
 relative dielectric constant at $20^\circ\text{C} = 1400$
 relative dielectric constant at $130^\circ\text{C} = 2100$

It is important to note that the dielectric constant, ϵ_r , the transmission sensitivity coefficient (deformation produced by 1 V), d_{33} , and the coupling coefficient (describing the efficiency to convert electric to acoustic energy), k_{33} , are all temperature dependent. Heating of the applicator occurs as some of the energy is reflected back due to acoustic impedance mismatch and changes of the optimal frequency during operation. When this energy exceeds the heat dissipation capacity of the casing and the surrounding metallic holder, the piezoelectric temperature increases substantially leading to significant deterioration of the acoustic output.

The coupling between the piezoelectric (5) and the acoustic transformer (7) is done with the silicone rubber Dow Corning RTV 3140 layer (6). Its thickness, calculated in appendix 4, is slightly larger than that given by the casing terminal edge (1'). This coupling layer must be free of air-bubbles.

The conversion of the longitudinal waves coming from the piezoelectric into surface modes going along the waveguide needle is done by the stainless steel 304 acoustic transformer (7). It is made up of several truncated cones ('stages') with exponentially decreasing diameters. The transformer design was based on the conical and exponential tapered horn theory [6]. Two- to six- stage transformers have been designed and tested. The acoustic transformer is the main part of the applicator, although the overall acoustic efficiency depends as well on the quality of the RTV coupling layer and the hard solder joint between the acoustic transformer and the terminating needle. An additional short cylindrical stage provides for matched transition from the acoustic transformer to the waveguide proper (8). This is a stainless steel spinal needle, which was soldered to the acoustic transformer. For the applicators I used, the waveguides and their unclad final radiative part called the antenna were of outer radius $R = 0.55 \text{ mm}$ (G19).

Applicators were held in position by a metallic holder, which was a solid aluminium plate with sets of holes 20 mm in diameter to contain various casing arrangements. The holder provided a passive heat dissipation through its own mass. The casings used for each applicator were about 20 mm outer diameter and this was the lower limit of the distance allowed between the applicators.

3.THEORY

3.1 Elastic and electroacoustics basic concepts

This section introduces the mechanics, acoustics and electroacoustics concepts directly relevant to the present study. The $\vec{}$ above will designate a vector, while $\hat{}$ will designate a tensorial or a matrix quantity. Notations are listed at the end of this chapter.

The stress $\hat{T}$ represents the force exerted per unit area. It is a symmetric tensorial quantity, which after renotation of significant elements for elastic solids reduces to a (6x1) matrix: three components correspond to compression-dilatation, and three to shear effects.

The strain $\hat{S}$ represents the fractional change of the solid length. For small values (displacements), stress and strain are related by the Hooke's law: $\hat{T} = \hat{c} \hat{S}$. For isotropic solids, the symmetric (6x6) stiffness tensor will have only 3 non-zero components, i.e c_{11} , c_{12} (for compressional effects) and c_{44} (for shear). Often, they are expressed by Lamé elastic constants λ_1 and λ_2 : $c_{11} = \lambda_1$, $c_{12} = \lambda_1 + 2\lambda_2$ and $c_{44} = \lambda_2$. Other elastic coefficients used to characterize materials are the Young modulus $E = T_3/S_3 = \lambda_2(3\lambda_1+2\lambda_2)/(\lambda_1+\lambda_2)$, and the Poisson ratio $\sigma = -S_1/S_3 = -S_2/S_3 = \lambda_1/[2(\lambda_1+\lambda_2)]$.

When a mechanical wave propagates into a medium, the particles of the medium will oscillate. For sinusoidal waves the temporal dependence can be separated as $e^{-i\omega t}$ yielding the spatial dependence of particle displacement $\bar{u}_p(\vec{r})$, and velocity $\bar{v}_p(\vec{r})$. Wave propagation can be described using the wavevector $\vec{k}$ of modulus $k = \omega/v = 2\pi f/v$, with f being the frequency and v the phase velocity in solid or liquid media.

Following the longitudinal wave vibration, particles in the medium have a velocity $\bar{v}_p$ related to the wavevector $\vec{k}_L$, frequency f , liquid density ρ_L and acoustic pressure p

(above the hydrostatic value) by [19]:

$$\bar{v}_p = p \bar{k}_L / (2\pi f \rho_L) \quad (2)$$

The resistance particles encounter during vibration is referred to as the acoustic (characteristic) resistance. Its real value is given by [19]:

$$Z_L = \frac{p}{v_p} = \frac{\omega \rho_L}{k_L} = v_L \rho_L \quad (3)$$

It is equivalent to the electrical resistance in an electric system.

Shear waves in the fluid medium exist only if the medium is viscous (i.e. gel phantom or brain, not in water). They are strongly damped away from the surface of the solid source [20]. The depth of penetration, defined as the distance the shear wave amplitude falls off by $e \approx 2.71$, depends on viscosity coefficients ν_L or η_L [20]:

$$d_{LS} = \sqrt{\frac{2\nu_L}{\omega}} = \sqrt{\frac{\eta_L}{\rho_L \pi f}} \quad (4)$$

For water (or extracellular fluid, cf. [28]) $\eta_L = 0.01$ g/cm s, while for high-viscous glycerine $\eta_L = 8.5$ g/cm s [20]. These values yield penetration depths at $f = 1$ MHz of 0.006 mm and 0.164 mm, respectively. Therefore, the direct shear effect may extend only few mm away from the needle even when the amplitude on the needle is large (the shear wave amplitude decreases about 300 times 2 mm into water).

In the case of longitudinal waves propagating in an infinite elastic solid of density ρ , the phase velocity is given by ([18],[19]):

$$v_I = \sqrt{\frac{c_{11}}{\rho}} = \sqrt{\frac{\lambda_1 + 2\lambda_2}{\rho}} \quad (5)$$

The corresponding acoustic characteristic impedance in the direction of propagation is

$$Z_I = \frac{\omega \rho}{k_I} = \sqrt{c_{11} \rho} = v_I \rho \quad (6)$$

Most of the medical ultrasonic devices (imaging, external radiators used in Doppler, hyperthermia or surgery systems) operate using only this type of wave. The loading in this case is real and has a resistive character.

Shear waves in isotropic elastic solids are of two types (there are two directions perpendicular to $\bar{k}_s$), but they propagate with the same velocity v_s [7]:

$$v_s = \sqrt{\frac{c_{44}}{\rho}} = \sqrt{\frac{\lambda_2}{\rho}} \quad (7)$$

The corresponding acoustic impedance is [18], [19]:

$$Z_s = \sqrt{\lambda_2 \rho} = v_s \rho \quad (8)$$

For semi-infinite elastic solids $v_s < v_I$ always, so $k_s > k_I$ and $Z_s < Z_I$ which are real values. However, more complicated propagation problems may admit complex solutions for the wavenumbers, corresponding to complex acoustic impedances Z .

3.2 Rayleigh type surface waves (RTSW)

Compressional and shear waves are basic modes, but many other types of modes may arise for a given propagation problem. A mode is specified by a propagation velocity (or wavenumber, given by the characteristic equation) and some physical quantities (particle displacement and velocity, stress, scalar and vector potentials, etc.) which may

be related to the specific boundary conditions.

The Rayleigh waves (proper) consist of two coupled longitudinal and shear modes propagating along a semi-infinite plane surface with the same velocity v_r . The rapid decay of both components within the volume is presented in fig.6. Particle velocity components described in fig.6a) have maximums around 0.2λ (with $\lambda \approx 3$ mm for Rayleigh waves at 1 MHz), while displacements, as showed in fig.6b), decay even faster. The Rayleigh wave propagation velocity is always smaller than v_s and for a material with Poisson ratio $0 < \sigma < 0.5$ it is approximately given by [6]:

$$\frac{v_r}{v_s} = \frac{.87 + 1.12\sigma}{1 + \sigma} \quad (9)$$

with values of the ratio between .87 to .96. For practical materials v_r can be found from fig.7, knowing σ and the longitudinal velocity (values are listed e.g. in ([9] pp.206-230)) first using eq.(10) to find v_s [19], and then using the ratio v_r/v_s and v_s in fig.7.

Figure 6:a) Particle velocity and b) displacement for Rayleigh wave on isotropic substrate [6]

Figure 7: Isotropic Rayleigh velocity for various longitudinal and shear velocities [6]

$$\frac{v_s}{v_l} = \sqrt{\frac{\lambda_2}{\lambda_1 + 2\lambda_2}} = \sqrt{\frac{.5 - \sigma}{1 - \sigma}} \quad (10)$$

The associated acoustic characteristic impedances along the z axis for longitudinal and shear components are ([7], p.107): $Z_{tl}=(\lambda_1+2\lambda_2)/v_t$ and $Z_{ts}=\lambda_2/v_t$.

The effect of Rayleigh waves propagating along curved (cylindrical) surfaces has been analyzed too ([5] pp.29-42). If the angular spatial wave period is comparable with the radius of curvature (very curly or along the circumference), an increased propagation velocity (up to $1.3v_r$, with v_r for the corresponding flat surface) may be encountered. For propagation along the cylinder generator the value is unchanged.

A slight change in v_r can be noticed when the solid is immersed into a liquid ([5] pp.46-57). There, plots of the relative velocity increase vs. the liquid/solid density ratio ρ_l/ρ are given for various Poisson ratios of the solid. When the density ratio is small the change in v_r is less than .5% (for water/steel interface it would be .125%). However, the liquid generally produces a large damping in amplitudes related to the leaking properties of Rayleigh waves [5].

For complex structures (such as the acoustic transformer and the terminal waveguide), some of the generated modes may have a Rayleigh wave like behaviour. In this case, the terminology Rayleigh type surface waves (RTSW) has been used [4].

The theoretical description below pertains to various parts of the IUWA: 1) the piezoelectric US source; 2) the RTV coupling layer; 3) the acoustic transformer; 4) the waveguide; 5) the pressure field within the liquid (water, gel phantom, brain).

3.3 The piezoelectric source

The thin piezoelectric disk radiating longitudinal waves into a resistive load is used by many US devices (e.g. [7]). The equivalent Mason electric circuit is showed in fig.8. It can be reduced to the clamped

capacity of the piezoelectric C_o , and the motional arm component describing electrical properties of the piezoelectric during vibration and characterized by resistance R_m and reactance X_m (inductive or capacitive). The C_o value calculated at 20°C was of 775 pF, while the measured value was around 1000 pF.

Figure 8: Mason electric equivalent circuit [7]

Piezoelectric coupling constant for a

transverse clamped disk (i.e no motion in the direction perpendicular to the electric field)

K_t is related to the electromechanical coupling coefficient from Table 1 by: $K_t^2 = K^2 / (1 + K^2)$. Also, at $f = 1$ MHz the longitudinal wavenumber in the piezoelectric material

satisfying $k_o l_o = \pi$ corresponds to a longitudinal velocity $v_l = 4060$ m/s, which was used

to calculate Z_o . For these conditions, if Z_o/Z_2 represents the ratio of piezoelectric impedance (complex)/acoustic load impedance (real or complex), the input impedance Z_3 can be simplified to [7]:

$$Z_3 = \frac{1}{j\omega C_o} \left[1 + \frac{4K_t^2}{\pi} \frac{Z_o}{Z_2} \right] \quad (11)$$

The power delivered by the source voltage V_g to motional arm of impedance Z_m is [7]:

$$P_m = \frac{Z_m |V_g|^2}{2 \left[(R_g + R_m)^2 + \left(X_m - \frac{1}{\omega C_o} \right)^2 \right]} \quad (12)$$

3.4 The coupling layer

The piezoelectric thickness tolerance given by the manufacturer is $\pm 6.25\%$. Due to these irregularities, the generated frequency lies within a bandwidth of (1.0000 ± 0.0625) MHz. In order to reach the steel transformer, the longitudinal wave has to go through the RTV-3140 coupling layer of thickness l_2 , as it

Figure 9: Propagation through the coupling layer

is presented in fig.9. At each of the contact surfaces, piezoelectric/RTV and RTV/steel acoustic transformer, some of the radiation will be reflected back. The acoustic impedance looking to the right from the point $z=0$ is ([7] p.23):

$$Z = Z_2 \frac{Z_3 + jZ_2 \tan k_2 l_2}{Z_2 + jZ_3 \tan k_2 l_2} \quad (13)$$

and the reflection coefficient (rc) at $z=0$ becomes ([7] p.23):

$$rc = (Z - Z_0) / (Z + Z_0) \quad (14)$$

Reflection is minimum for $k_2 l_2 = \pi, 2\pi$, etc., and in practice a half wavelength thickness layer was used. A reflection will always take place although the frequency uncertainty allows a certain margin of tolerance for k_2 and l_2 . This effect depends on the impedance

mismatch between the piezoelectric and the acoustic transformer (Z_0 and Z_3) and is presented in Appendix 4. Air bubbles within the RTV layer would mean $Z_2 = Z_0 = 0$, i.e. acoustic short circuit and total reflection of the incident wave.

3.5 Propagation in the acoustic transformer

When impinging on the outer surface of the acoustic transformer (locally a plane steel/air boundary), the acoustic waves are geometrically described by the Snell's law:

$$\frac{\omega}{v_1} \sin \theta_1 = \frac{\omega}{v_1'} \sin \theta_1' = \frac{\omega}{v_s} \sin \theta_s \quad (15)$$

On each incidence at the free lateral boundary, a continuous conversion of longitudinal wave into shear wave and reciprocal occurs ([6] pp.2-6, 30-38). It is believed that also part of each wave will be converted into a surface wave, but this hypothesis is to be proven. For steel longitudinal velocity $v_l=5600$ m/s and shear velocity $v_s=3200$ m/s, and the longitudinal velocity in air $v_l'=340$ m/s, the only critical angle (when total reflection takes place) may happen when shear waves are converted to longitudinal waves in steel,

Figure 10: Single initial longitudinal ray propagating through the 5 stages transformer

i.e for a shear wave incidence angle $\theta_s=39^\circ$. This condition is very likely to be fulfilled somewhere along the acoustic transformer. The emergent longitudinal wave (called

evanescent in [6]) will propagate along the generator, constituting the 0 mode of RTSW when it eventually reaches the waveguide. Reciprocally, a conversion of surface into longitudinal/shear (volume) waves may take place at edges ([5] pp.42-46) or due to surface defects ([5] pp.57-65). This will attenuate the propagating surface mode especially at the joints between adjacent truncated cones. Also, the ray diagram presented in fig.10 shows that some of longitudinal waves propagating within the actual 5-stages acoustic transformer will be lost as they return toward the piezoelectric. The problem of a quantitative theoretical description of the efficiency of the surface modes generation into the truncated conical acoustic transformer is still open because of its complexity.

3.6 Modes in the acoustic transformer and the waveguide

The few known studies presenting elastic waves in truncated cones ([21], [29]) consider mostly longitudinal waves and don't give a theoretical solution for the above geometry. Modes in elastic cylinders have been thoroughly analyzed ([6], [22]), while the propagation of surface waves along elastic cylinders has been reviewed in [13]. Therefore, exact formulae were available only for the cylindric waveguide (i.e the 1.1 mm diameter part of the acoustic transformer and the needle), while the actual modes in the rest of the transformer could be only speculated on.

The modes in an elastic cylinder can be found by solving the wave equation for the scalar Φ and the vector $\bar{\Psi}$ displacement potentials ([6] pp.105-114)

$$\nabla^2 \Phi + \frac{\omega^2}{v_l^2} \Phi = 0 \qquad \nabla^2 \bar{\Psi} + \frac{\omega^2}{v_s^2} \bar{\Psi} = 0 \qquad (16)$$

in cylindrical coordinates with the appropriate boundary conditions for stress. Following

the very detailed discussion given in [22], the general frequency equation for modes can be reduced to particular cases giving the family of torsional, longitudinal, and flexural modes. Branches of these modes, presented in fig.11, show the reduced angular frequency $\Omega=2\pi fR/v_s$ vs. the reduced propagation constant kR (where k is in the axial direction).

For the cylinder radius $R = 0.55$ mm and the frequency $f = 1$ MHz, only the $F(1,1)$ flexural mode may exist. In fig.11 the value $\sigma = 0.3317$ gives a ratio of flexural/shear velocities $v_r/v_s = \Omega/(kR) = 0.93$, identical to the value given by the eq.(9) for Rayleigh wave velocity. This implies that the $F(1,1)$ mode is a surface wave under the specified conditions, corresponding to the $n=1$ cylindrical surface component described in [13].

Figure 11: Low-order flexural modes family for elastic cylinder with $\sigma=.33$ [22]

A discussion of surface modes on rods [13] shows that these modes can propagate for frequencies above a threshold cut-off frequency, f_n . Its value depends on the material on which the RTSW propagates and the cylinder radius R , and f_n is given by [13]:

$$f_n = \frac{nv_r}{2\pi R} \quad (17)$$

The wavenumber k_{zz} along the cylinder generator direction is given by [13]:

$$k_{nz} = \frac{2\pi f}{v_r} \left[1 - \left(\frac{\pi v_r}{2\pi f R} \right)^2 \right]^{1/2} \quad (18)$$

The mode will propagate along helical paths making an angle θ_n with the generator [13]:

$$\theta_n = \arcsin \left[\frac{\pi v_r}{2\pi f R} \right] \quad (19)$$

For the conditions presented above, these formulae yield values listed in Table 2.

Table 2 RTSW mode specifications on the 0.55 mm radius steel waveguide at 1 MHz.

n	0	1	≥ 2
f_n , MHz	0	.81	$1.62 > 1$
θ_n , °	0	60	
k_{nz} , mm^{-1}	2.244	1.315	
$k = k_{nz} / \cos \theta_n$, mm^{-1}	2.24	2.24	
$\delta_{nz}/2 = 2\pi/2k_{nz}$, mm	1.4	2.4	

Surface wave modes with $n \geq 2$ won't propagate along the needle for the given conditions (radius, material), as the cut-off value is above the frequency used. From these values, the mode $n=0$ can propagate along the needle generator, with v_r for flat surfaces. When the mode propagates along the transformer, it approaches the edges between cones perpendicularly so it will be attenuated. The mode $n = 1$ propagates along a helical path [13] on the waveguide, and, possibly, with an increased curliness on the narrower cones of the transformer. Its axial periodicity constant $\Delta_1 = \delta_{1z}/2 = 2.4$ mm (considered half δ from the intensity standpoint) is within the observed range, as will be discussed later. Due to the oblique angle it approaches edges it will be less attenuated and also a possible better absorption into the liquid makes this RTSW mode the dominant one. The fact that

both RTSW modes have the same wavenumber k but different ways to propagate on the needle surface suggests a kind of degenerate states of a unique type of wave, i.e of the surface wave. However, they cannot be considered as harmonics, as they have different genesis not being proper Rayleigh waves.

The axial periodicity constant, Δ_0 , is sensitive to frequency changes. For $v_r = 2800$ m/s and $R = 0.55$ mm, the mode $n = 0$ at $f = .9355$ MHz will be axially exactly packed within the $n = 1$ mode as $\Delta_0 = .5\Delta_1$. This may operate as a waveguide resonance condition, giving a possible explanation why in several cases the best operating frequency was found around .940 MHz. If this is the case, the piezoelectric frequency f , the needle radius R and the material Rayleigh velocity v_r are found to satisfy the following relation such that modes 0 and 1 in steel cylinder yields the resonance of the waveguide:

$$f = v_r / (\pi \sqrt{3} R) \quad (20)$$

For the mentioned conditions, the calculated radius would be .51 mm. Matching the waveguide resonance frequency to the piezoelectric resonance value may lead to an increased applicator output. However, a decrease in the needle radius implies an increased divergence of the emitted radiation, which would lead to smaller source generation regions around each of the applicators. A trade-off between the maximum radius allowed by clinical considerations, needle material acoustic properties and frequency should be achieved in order to have a maximum output from each waveguide.

3.7 Acoustic field in liquids

At the distal end of the transformer and on the part of the needle in contact with the air, most of the waves are RTSW, either of evanescent or of flexural nature. For the

immersed part (antenna) of the needle, equations (16) for the cylindrical steel waveguide should be supplemented by (subscript L stands for liquid):

$$\nabla^2 \Phi_L + \frac{\omega^2}{v_L^2} \Phi_L = 0 \quad (21)$$

and different boundary conditions have to be applied ([4]). The real solution of the dispersion equation is the Stoneley wave (evanescent wave in liquid, related to RTSW on solid). For $v_r < v_s$ and density ratio (solid/liquid) restrictions fulfilled by liquid densities close to 1 g/cm³ ([14]), there is another complex solution describing a RTSW continuously leaking energy into the liquid.

A theory of cylindrical sources radiating outgoing waves into a liquid is given in [8], [16] and [17]. For the case discussed here the following apply:

a) the length of the source can be approximated as infinite: in practice, this is fulfilled if the antenna length L equals about 10 or more axial periodicity constants, Δ .

b) there is an axial periodicity; for the allowed surface modes $n = 0, 1$ for stainless steel needle at 1 MHz, the axial properties are described in table 2.

c) an axial symmetry is assumed, with the acoustic pressure $p = p(r, z)$.

d) the sound propagation velocity in the medium is 1500 m/s, yielding at $f=1$ MHz the wavenumber $k_L = 4.19 \text{ mm}^{-1}$; this velocity is true for water and (approx.) Aquasonic gel, but not necessarily for other media. With re-notation $k_o = k_{oz}$ and $k_l = k_{lz}$ in Table 2 (describing the axial periodicity), we are in the case $k_L > k_o$ and k_l , which corresponds to a cylindrical source leaking energy outward [16].

Adapted to our two-surface-mode situation without angular dependence, the

general acoustic pressure field formula is ([8] p.168):

$$p(r,z) = -\rho_L \left\{ \sum_{n=0,1} \frac{W_n H_0[(k_L^2 - k_n^2)^{1/2} r]}{(k_L^2 - k_n^2)^{1/2} H_0'[(k_L^2 - k_n^2)^{1/2} R]} \cos(k_n z) \right\} \quad (22)$$

Here, W_n are constants, $H_0 = J_0 + jY_0$ is the Hankel function of the first kind of zero order, J_0 and Y_0 are the Bessel functions of the first and the second kind, and the Hankel function arguments are always real. On the surface of the antenna $r=R=0.55$ mm, the acoustic pressure is given in terms of modal acoustic impedances Z_0 and Z_1 ([8], pp.168-173), both having a real (resistive) and an imaginary (reactive and positive, due to the accession to inertia) component. In the approximation of the Hankel function argument at $r = R$ e.g. $(k_L^2 - k_n^2)^{1/2} R$ much greater than $(n^2 + 1)$, the formulae to give the resistive component r_n and the accession to inertia (being the equivalent of an induction L in an electroacoustic system) m_n for $n = 0, 1$ are ([8], pp.172 and 169):

$$r_n = \rho_L v_L \quad m_n = \frac{\rho_L}{2R(k_L^2 - k_n^2)} \quad (23)$$

The units are $[g/cm^2s]$ for r_n and $[g/cm^2]$ for m_n , therefore the inductive reactance would be $2\pi f m_n$. In order to compare them I followed [8], where the specific acoustic resistance and respective reactance are defined as non-dimensional quantities $(r_n / \rho_L v_L)$ and $(m_n k_L / \rho_L)$. In [16], plots of these quantities against the non-dimensional $(k_L R)$ are given for various ratios of $(\delta_{az}/2R)$. Results for applicators are summarized in Table 3. Values in lines 1-4, 6-7 and 9-11 were calculated with $v_L = 1500$ m/s, $f = 1$ MHz, $k_L = 4.189$ mm⁻¹, $R = .55$ mm, $k_L R = 2.3$. Lines 5 and 8 were read from the graph in [16].

Lines 3 to 8 suggest that the values of the specific acoustic impedances (resistive

or reactive) should be between the calculated and the ones read from fig.2g and 2h in [16]. The two impedances have comparable values, and the large acoustic mass reactance may be accountable for the limiting effects observed during the trial with shifting the operating frequency.

Table 3: Properties of the outgoing compressional wave into the liquid

#	n	0	1
1	k_n , mm^{-1} (on the needle surface)	2.244	1.315
2	$(k_L^2 - k_n^2)^{1/2} R$, compared with $(n^2 + 1)$	1.95 > 1	2.19 > 2
3	acoustic resistance r_n , eq.(23) ($\times 10^5 \text{g/cm}^2\text{s}$)	1.5	1.5
4	resulting $r_n/\rho_L v_L$ from equation above	1	1
5	same as above, from graph loc.cit.	-	1.2
6	acoustic reactance from (23), ($\times 10^5 \text{g/cm}^2\text{s}$)	.46	.36
7	resulting $m_n k_L/\rho_L$ from equation above	.30	.24
8	same as above, from graph loc.cit.	-	3.0
9	outgoing angle $\gamma_n = \arccos(k_n/k_L)$, °	64	80
10	radial phase velocity v_{Ln} , m/s	1500	1827
11	radial absorbtion coefficient a_n , cm^{-1}	.25	.32

The leaking surface modes propagate in the irradiated medium as compressional waves at an angle γ_n with the wave vector $\vec{k}$ ([6], pp.283-286), ([8] p.173), and [15]). This angle is given in the row #9. It should be observed that both surface modes have the same wavenumber k but different propagation (straight along the needle, or curly). This leads to different radiative properties into the liquid (directions and absorption coefficients). Also, the leaked conical waves do not have necessarily the same amplitude in the forward and the backward direction, and the standing waves in the waveguide

might have a preferential direction.

The normal component of the wave in the medium will propagate into the medium with a radial phase velocity [16] v_{Ln} (where λ_L is the sound wavelength in the medium at 1 MHz, $\lambda_{Ln} = 1.5$ mm for $v_L = 1500$ m/s):

$$v_{Ln} = \frac{v_L}{[1 - (\frac{n\lambda_L}{\Delta_n})^2]^{1/2}} \quad (24)$$

The acoustic pressure of the outgoing wave, cf. [16], would decrease radially as $r^{-1/2}$, the dependence characterizing a cylindrical wave and leading to radiated intensity divergence proportional to $1/r$. The absorption coefficient (in [Np/cm]) of the normal-to-needle component of the Rayleigh type wave at high frequencies would be [15]:

$$a_n = \frac{f\rho_L v_{Ln}}{\rho v_r^2} = \frac{\rho_L k^2}{2\pi\rho k_{Ln}} \quad (25)$$

The corresponding values for $n = 0, 1$ are given in the row #11. These values are several times higher than the absorption coefficients given in literature for ultrasound longitudinal waves in brain [23]. Previous measurements in this lab showed similarities of the absorption properties of Aquasonic gel and tissue *in vitro* when IUWA applicators were used [2]. This implies that there is a difference in the acoustic absorption of the ultrasound from the present applicator and other ultrasound devices.

However the results obtained with eq.(25) are questionable for two reasons. First, for a given applicator (k, ρ) this equation gives the same value for Aquasonic gel and water, although they have very different elastic properties. Secondly, if this were true, then the ratio of the initial heating rates (IHR) in gel and water would be given by the

inverse ratio of their specific heats $c_{\text{water}}/c_{\text{gel}}$. A rough estimate of c_{gel} indicates that $c_{\text{gel}}/c_{\text{water}} \approx 1.4$ but experiments indicate that the IHR for gel is orders of magnitude higher.

A remark about the outgoing tangential component: for a very viscous medium, this component would produce shear waves with reduced amplitudes even relatively far away. At 6 mm away from the needle in glycerine, eq.(4) gives 1% of the original shear amplitude. The attenuation coefficient formula for this case given in [15] leads to unrealistic small values. This coefficient should be larger than that for the compressional component, as shear wave is more confined. Therefore within a few mm from the antenna, the overall absorption and attenuation coefficients may be expected to be higher than in further regions because of the combined presence of compressional and shear radiation.

Due to the complex wave generation process (piezoelectric emission, transmission through the layer, mode conversion in the transformer, and propagation along the waveguide with radiation of energy), usually several enhanced output signal frequencies will be detected in the medium. They range from 0.930 to 1.070 MHz and can be partly explained by different imperfections in applicator structures due to manufacturing (piezoelectric and RTV layer thickness variations, alignment, eccentricity, gluing, soldering, surface defects, etc). The largest amplitude output signal at a given voltage across the piezoelectric was used for producing hyperthermia and will be called further as the operating frequency (OF).

3.8 Acoustic intensity

The acoustic pressure is related to changes in the local density of the medium. To

describe this pressure field, a hydrophone connected to a spectrum analyzer has been used. Theoretically, the hydrophone signal is related to the spatial peak-temporal average intensity (I_{SPTA}) for a fixed beam averaged over a temporal period [24] and in the case of experiments described here, it was

Figure 12: Geometry for local and average intensity

proportional to the absolute value of the acoustic pressure at that point. The hydrophone signal does not give the instantaneous pressure but it follows the temporal variations of the pressure for times greater than $1/f = 1\mu\text{s}$.

Assuming axial symmetry, local pressure, p , in cylindrical coordinates is a function of (r, z) . This pressure squared (proportional to the hydrophone signal squared) will be referred to as the local intensity $I(r, z)$. The local intensity represents the power dP across the elemental cylindrical band of radius r and height dz . The corresponding geometry is presented in fig.12. For this case $I(r, z)$ can be expressed as:

$$I(r, z) \sim [p(r, z)]^2 \sim [\text{signal}]^2 = \frac{dP}{2\pi r dz} \quad (26)$$

For $r = \text{constant}$ (all axial pressure measurements have been done at 2.04 mm from the needle) local intensity integrated over the antenna length L will be referred to as the integrated intensity (II). This quantity divided by L gives the average intensity over that particular surface r , $\langle I \rangle_r$. The average intensity multiplied by the total lateral surface ($2\pi r L$) gives the power across that surface, P_r . For fixed r , both P_r and/or II (as being

proportional to P_r) characterizes the power of the applicator.

Correcting for divergence and the antenna's length, $I(r,z)$ at $r \geq R$, $0 \leq z \leq L$ is [1]:

$$I(r,z) = B \frac{L_0}{L} \sin^2(2\pi \frac{z}{\delta_n}) e^{-\nu z} \frac{R}{r} e^{-\mu(r-R)} = B \frac{L_0}{L} \cdot I(z) \cdot I(r) \quad (27)$$

In the above expression, R/r describes the radial beam divergence term. The axial pressure periodicity constant δ_n is twice the value of the axial intensity periodicity constant Δ_n ; the latter describes the axial hydrophone signal periodicity as well. The subscript n stands for the hypothesized two possible modes on the antenna. The observed axial intensity attenuation constant, ν , indicates possible intensity variations in axial direction due to surface defects, antenna's end or cladding ring. The length correction L_0/L (with $L_0=1.5$ cm being the typical antenna length used) tells that L bigger than L_0 would reduce the intensity at a point. If it is not specified otherwise, the length $L = L_0 = 1.5$ cm has been used and ratio becomes 1. The value of the radial power attenuation coefficient μ has been considered to be close to values from Table 3, although next to antenna values may be bigger.

To convert the hydrophone signal into acoustic pressure and then into intensity, a hydrophone calibration has to be done first. This means to correlate the absolute output squared found by combining the hydrophone signal with the spectrum analyzer sensitivity with the power emitted into the medium by the given source under specific conditions. In [2], this power has been estimated for a planar source from radiation balance measurements. Based on the hydrophone calibration, the measured signal at the distance r from IUWA's needle was converted into power and divided by the lateral surface of the

antenna. Following this procedure, the intensity at the needle surface for that particular case was reported to be 0.076 W/cm^2 [2], which leads to $B = 0.152 \text{ W/cm}^2$.

The intensity in (27) has been expressed in terms of axial and radial dependence. As pointed out in [1], the axial temperature variation pattern doesn't follow the axial pressure variations. Thus only axial average intensity, $\langle I(r) \rangle_z$ can be used for further temperature calculations and the z dependence can be eliminated. Averaging $I(z)$ in (27) with $\langle \sin^2 \rangle = 1/2$ and $v = 0$ (the approximation used throughout this study) and ignoring the length correction, the simplified formula for the intensity showing only radial dependence at $r \geq R$ would be:

$$\langle I(r) \rangle_z = \frac{B \cdot R}{2 \cdot r} \cdot e^{-\mu(r-R)} \quad (28)$$

At the needle, $r = R$ and (28) becomes $\langle I(R) \rangle_z = I_o = B/2$. Thus, the constant B is twice the average intensity at the antenna surface.

3.9 Source term

The acoustic intensity multiplied by the power absorption coefficient, a , gives the rate of heat generation per unit volume. In the following it will be referred to as the source term (ST) and denoted by g . The radial ST averaged over z is:

$$\langle g(r) \rangle_z = a \cdot I_o \cdot \frac{R}{r} \cdot e^{-\mu(r-R)} \quad (29)$$

With the notation $\langle g(R) \rangle_z = g_o$ for the ST on the needle, where

$$g_o = a \cdot I_o \quad (30)$$

the equation (29) can be rewritten as:

$$\langle g(r) \rangle_z = g_o \cdot \frac{R}{r} \cdot e^{-\mu(r-R)} \quad (29')$$

In the latter, the ratio represents the divergence term due to the spreading of the wave, while the exponential describes the attenuation similar to the plane wave.

Although only the spatial variables have been discussed, the temperature increase varies also with time for $t \gg 1/f = 1\mu s$. The ST can be used to evaluate the initial heating rate (IHR) at a point $r > R$. The theoretical basis of the evaluation is presented in [25] and it has been specified for conditions applicable in the studied case as [2]:

$$\left[\frac{\partial \tau(r)}{\partial t} \right]_{t=0} = \frac{\langle g(r) \rangle_z}{\rho_L c_{mL}} \quad (31)$$

The subscript L stands for liquid and c_{mL} is the mass specific heat capacity [J/g°C].

3.9.1 Analysis of the source term

The power deposition into the phantom is different when it comes only from contact with a hot surface at the source and when, in addition, the extended source radiates energy within the medium. The source term is the difference between heating using IUWA ("active heating", [30]) and only conductive with hot water tubes, resistive heating etc. ("passive heating", [30]). Notation of $g(r)$ in (29) will be simplified as:

$$\langle g(r) \rangle_z \equiv g(r) = g_o \cdot \frac{R}{r} \cdot e^{-\mu(r-R)} \quad (29'')$$

Individual roles of divergence and attenuation can be better distinguished in 'the percent source' term, %g. This can be defined as the ratio of the source term at any r to its value at $r=R$:

$$\%g = \frac{R}{r} \cdot e^{-\mu(r-R)} \quad (32)$$

The plot of the function $\%g(r)$ with radial distances up to 12 mm away from the antenna surface is given in fig.13. This figure demonstrates the decrease in the value of $\%g$ with the increasing distance from the needle ($r-R$). For numerical estimations, the attenuation was varied from $\mu=0$ (unattenuated wave, just divergence) to $\mu=3 \text{ cm}^{-1}$ (extremely attenuated, depth of penetration = 3.3 mm). Typical value at 1MHz for the attenuation coefficient for ultrasound delivered by external applicators is $\mu=0.1 \text{ cm}^{-1}$, while for leaking surface waves it might be higher (see section 3.7).

At high $\%g$, its values do not differ much for the five attenuations. The $\%g$ decreases fast falling 2.7 times (to about 37% of the initial value) at a distance of the order of 1 mm from the needle surface. Even at distances where $\%g$ is small, typical values of μ for biological tissues do not affect significantly the source term. At 10 mm

Figure 13: $\%g$ vs. radial distance

where $\%g$ is already small (around 5% of the value at the antenna surface) the difference between these small $\%g$ values for $\mu=0$ (dots) and $\mu=0.1 \text{ cm}^{-1}$ (solid) is 10%. In simulations, values of the source term less than 5% were ignored. Thus, for interstitial ultrasonic applicators with cylindrical divergence the attenuation in the source term can

be quantitatively neglected.

As almost all the radial dependence of $\%g$ comes from the divergence term R/r , its variation with antenna radius R is illustrated in fig.14 for $\mu = 0.1 \text{ cm}^{-1}$. This figure shows that $\%g$ at a given distance from antenna increases with increasing R . Numerical comparison of $\%g$ for two different R_1 and R_2 and same μ shows that percentage source term ratio is independent on the distance r . For example, an increase from $R_1 = 0.55 \text{ mm}$ to $R_2 = 0.65 \text{ mm}$ yields an 18% increase of $\%g$ at any distance r , while a change from $R=0.55 \text{ mm}$ to $R=1.00 \text{ mm}$ results in about 83% increase of $\%g$.

Fig. 13 shows that at distances greater than about 1 mm $\%g$ falls to relatively low levels. Yet, as it will be shown in simulations for array of several IUWA, these levels produce a very significant advantage of active over passive heating. Table 4 presents penetration depths for plane waves (which

Figure 14: $\%g$ for several needle radius R with $\mu=0.1 \text{ cm}^{-1}$

are reciprocals of attenuation coefficients) and for cylindrical sources (e.g fig.13, where divergence predominates) specifying the value $r_{\%g=0.05}$. This is the distance where $\%g$ falls to 5% of its maximum value which was considered as the lower threshold for simulations. As expected, the source region shrinks down for large values of μ but at $\mu = 0.1 \text{ cm}^{-1}$ the just-divergence approximation holds within 10% approximation.

Table 4: Attenuation and divergence effects for planar and cylindrical sources

μ [cm^{-1}]	0.0	0.1	0.3	0.8	3.0
penetration depth plane wave [mm]	∞	100	33	12.5	3.3
penetration depth cylindrical [mm]	0.95	0.94	0.93	0.90	0.80
$r_{0.05}$, cylindrical source [mm]	10.5	9.5	8.0	6.1	3.4

Relationships presented in the last sections suggest several ways to increase the absorbed intensity at the antenna surface, g_o . This can be done by increasing the absorption coefficient, a , for example by increasing the frequency of the radiated waves. If this were done, the problem of additional surface modes on the waveguide should be considered. Other ways to increase I_o would be by improved manufacturing of IUWA, by supplying more voltage on piezoelectric plates or by using piezoelectrics with a larger radiating surface. These methods can be combined with a larger radius of the antenna, R , which would increase the divergence. Larger radius might allow additional surface modes to develop with higher cut-off frequency.

3.10 The effective thermal conductivity equation (ETCE)

Temperature distribution within the absorbing tissue sample can be obtained from the bio-heat transfer equation. If the blood perfusion term is included in thermal conduction coefficient ($k = k_{\text{eff}}$) the approximation of the former equation is known as 'the effective thermal conductivity equation' (ETCE) [32]. It can be written as:

$$\frac{\partial^2 \tau}{\partial r^2} + \frac{1}{r} \frac{\partial \tau}{\partial r} + \frac{\partial^2 \tau}{\partial z^2} + \frac{g(r,z)}{k_{eff}} = \frac{1}{\lambda_{eff}} \frac{\partial \tau}{\partial t} \quad (33)$$

For a single IUWA, the z averaging of the source leads to a non-homogeneous 1-D transient problem, which can be solved analytically (e.g [2]). ETCE can be written as:

$$\frac{\partial^2 \tau}{\partial r^2} + \frac{1}{r} \frac{\partial \tau}{\partial r} + \frac{\langle g(r) \rangle_z}{k_{eff}} = \frac{1}{\lambda_{eff}} \frac{\partial \tau}{\partial t} \quad (33')$$

In a discussion of the steady state the transient-temporal dependence can be ignored and (33') becomes a second order differential equation. It has been solved in Appendix 1 as a test problem to check out the accuracy of finite element method (FEM).

For an array of N IUWAs the problem becomes 2-D with the steady-state ETCE of the form:

$$\frac{\partial^2 \tau}{\partial x^2} + \frac{\partial^2 \tau}{\partial y^2} + \frac{\sum_{i=1}^N \langle g_i \rangle_z}{k_{eff}} = 0 \quad (33'')$$

An analytic solution of eq.(33'') appears to be quite cumbersome. Instead, FEM simulations have been carried out. The ALGOR software was used to obtain steady-state solution which corresponds to the final state of thermal equilibrium. The meshing of the solution domain had the applicators as internal boundaries and the phantom wall as the outer boundary. The boundary conditions envisaged for a single applicator ([1],[2]) can be extended to multiple applicators case as:

- a) initial condition: 0°C at $t=0$ everywhere.
- b) temperature elevation of τ_i at each antenna surface.
- c) temperature elevation of τ_o at the phantom lateral wall.

The solution of the 2-D problem will be graphically displayed as a temperature map $\tau(x,y)$. Temperature on the needles was assumed to be higher than the temperature on the closest thermistor and this assumption was checked by the comparison of experimental and simulated results.

3.11 Temperature elevation plateau

Patterns of single IUWA temperature increase in time were originally presented in [3]. For a fixed average power at antenna surface, P_o , the temperature at a point in the medium rises exponentially reaching a constant plateau value, τ_p , in the time interval Δt_p . This plateau temperature indicates an equilibrium between the energy delivered by the antenna and converted into heat in the phantom and the heat lost by the phantom. The above applies to several IUWAs operated simultaneously, although in that case the temperature distribution loses its symmetry.

Curves (1) and (2) in fig.15 describe two possible 'exponential patterns' for IUWA driven at high and low power, respectively. The low power P_{o2} doesn't generate much temperature elevation (low τ_{p2}) but is fast (small Δt_2). For same conditions of irradiation, the larger temperature elevation plateau τ_{p1} requires both P_{o1} and Δt_{p1} to have bigger values. The time Δt_{p2} can be shortened if the

Figure 15: Plateau at two powers P_o

initial heating takes place with P_{o1} but once the desired τ_{p2} is achieved, the power is

decreased to P_{o2} . Such case is described by the curve (3) and this was the procedure used in all measurements presented in this study. The heating pattern (3) is not exponential and it combines the initial power $P_{o1} = P_{oi}$ with the final power $P_{o2} = P_{of}$ in order to get a lower-than-maximum temperature elevation plateau τ_{o2} in a shorter interval of time $\Delta t_p = \Delta t_{p3} < \Delta t_{p2} < \Delta t_{p1}$. From this standpoint, P_{oi} is desired to be as high as possible, this shortening the time in which the plateau can be achieved. For a given phantom (volume, conductivity), a trade-off between P_{oi} , τ_p and Δt_p occurs. If phantom has density ρ and specific heat c_m , P_{of} on each needle at plateau is related to the average temperature increase τ_a over the whole volume V by:

$$N \cdot P_{of} \cdot \Delta t_p = \rho \cdot V \cdot c_m \cdot \tau_a \quad (34)$$

where N is the number of applicators in the array. For a given power on each needle, the plateau temperature elevation is inversely proportional to the phantom volume and directly proportional to the number of IUWAs in array and the time Δt_p .

3.12 Notations and summary

The following notations, appearing in *italic* in the formulae, were used throughout this chapter:

A_o - piezoelectric radiating area;

a , a_n - ultrasound power absorption coefficient, [Np/cm] or [cm⁻¹];

α - amplitude attenuation coefficient; $\mu = 2\alpha$;

B - intensity constant, [W/cm²];

c_m , c_{mL} (c_v) - mass (volumic) specific heat capacities;

C_o - clamped electric capacity of the piezoelectric;

$\hat{c}$ - elastic stiffness tensor, [N/m²]; has elements c_{11} , c_{12} and $c_{44} = \lambda_2$;

d_{LS} - depth of penetration of shear wave in liquids;

$\delta_{nz} = \delta_n$ - pressure axial periodicity constant, [mm]; specific for surface mode n ;

Δ_n - intensity axial periodicity constant; $\Delta_n = 2 \delta_n$;

E - Young modulus of elasticity, [N/m²];

η_L - dynamic viscosity coefficient of a liquid, [g/cm s];

$\epsilon_{o,r}$ - piezoelectric dielectric constant;

f - US frequency used;

f_n - cut-off frequency for surface modes;

Φ , Φ_L - scalar displacement potential function, in solid and liquid;

$g(r,z)$ - local source term;

$\langle g(r) \rangle_z$ - source term, [W/cm³]; is local ST averaged in z -direction;

$g_o = \langle g(R) \rangle_z$ - source term at the needle surface;

$\%g = g/g_o$ - percentage source term;

γ_n - radiating angle;

H_0 - Hankel function of first kind, zero order;

$I(r,z)$ - local intensity, [W/cm²];

II - integrated intensity;

$\langle I \rangle_r$ - average intensity, for power P_r crossing the surface of radius r and height L ;

$\langle I(r) \rangle_z$ - local intensity averaged in z -direction;

$I_o = \langle I(R) \rangle_z$ - average intensity at the needle surface;

k_o - wavenumber for ultrasound in piezoelectric;

k_2 - wavenumber for ultrasound in RTV layer;

$k_n = k_{nz}$ - wavenumbers for surface modes in z-direction;

k_l - wavenumber of longitudinal wave in solids;

k_s - wavenumber of shear wave in solids;

k_L - wavenumber of longitudinal wave in medium;

$(k_{eff}), k$ - (effective) thermal conductivity coefficient of the medium, [W/cm°C];

K_t - piezoelectric transverse coupling coefficient;

K - piezoelectric electromechanical coupling coefficient;

χ_{eff} - effective thermal diffusivity coefficient, [cm²/s]; $\chi_{eff} = k_{eff}/c_v$;

L - length of the antenna;

L_o - length of antenna during calibration (typical length, 1.5 cm);

l_o - piezoelectric thickness; $l_o = \lambda/2$;

l_2 - thickness of the RTV layer;

λ - wavelength;

λ_L - wavelength of radiated wave into the medium;

λ_1, λ_2 - Lamé elastic constants (often referred to as λ and μ);

m_o - modal inductive component of the medium acoustic impedance, [g/cm²];

μ - radial power attenuation coefficient, [cm⁻¹];

n - surface mode number;

N - number of IUWAs in array;

ν - axial intensity attenuation constant (along the antenna), [cm⁻¹];

ν_L - cinematic viscosity coefficient of a liquid, [cm²/s];

Ω - reduced angular frequency for the waveguide;

ω - angular velocity;

$p(r,z)$ - acoustic pressure; at coordinates (r, z) ;

P - acoustic power;

P_o, P_{oi}, P_{of} - z-averaged radiated acoustic power at the antenna surface ($P_{r=R}$);

P_r - acoustic power involved in $\langle I \rangle_r$;

P_m - power delivered by the electric source to the motional arm of the piezoelectric;

$\bar{\Psi}$ - vector potential displacement;

r - radial distance;

$r_{0.05}$ - distance from IUWA beyond which ST has been ignored, as $\%g < 5\%$.

r_n - modal resistive component of the medium acoustic impedance, $[g/cm^2s]$;

R - antenna radius, 0.55 mm;

R_g - electric source output resistance, 50Ω ;

rc - reflection coefficient;

ρ, ρ_L - mass density of the elastic medium;

$\hat{S}$ - strain tensor, has elements S_1, S_2 and S_3 ;

σ - Poisson ratio;

$t, (\Delta t_p)$ - time (interval);

T - actual temperature of the absorbing substance;

T_o - surrounding (initial) temperature;

$\tau = T - T_o$ - temperature elevation;

τ_a - average temperature increase over the phantom volume;

τ_i (τ_o) - inner (outer) boundary temperature elevations;

$\hat{T}$ - stress tensor, [N/m²]; contains element T_3 ;

$\theta_n, \theta_t, \theta_p, \theta_c$ - propagation angles;

$\bar{u}_p$ - particle displacement in the medium;

$\bar{v}_p$ - particle velocity vector;

V - phantom volume;

V_g - electric source voltage;

v_l - longitudinal phase velocity in solids;

v_s - shear phase velocity in solids;

v_L - longitudinal phase velocity in liquids;

v_{Ls} - shear phase velocity in liquids;

v_1' - sound wave in air, 340 m/s;

v_r - Rayleigh wave phase velocity;

v_{Ln} - normal component of compressional wave velocity radiated into the medium;

W_a - constant;

R_m, X_m - piezoelectric motional arm resistance, reactance;

z - axial distance, for coordinate system see fig.5.

Z - impedance beyond the RTV layer;

$Z_m = R_m + j X_m$ - impedance of the piezoelectric motional arm;

Z_o - piezoelectric impedance;

Z_2 - impedance of the RTV layer;

Z_3 - impedance beyond the acoustic transformer;

Z_l - acoustic impedance for longitudinal wave propagating into a solid;

Z_s - acoustic impedance for shear wave propagating into a solid;

Z_L - acoustic impedance for longitudinal wave propagating into a liquid;

Z_{rl} , Z_{rs} - acoustic impedance for longitudinal and shear components of Rayleigh wave;

The following equations were used in the next chapters of the thesis:

The acoustic intensity at a point in the medium is given by:

$$I(r,z) = B \sin^2\left(\pi \frac{z}{\Delta_1}\right) \cdot e^{-\nu z} \cdot \frac{R}{r} \cdot e^{-\mu(r-R)}$$

Radial dependence of the z-averaged source term is defined by divergence and attenuation and can be written as:

$$\langle g(r) \rangle_z = g_o \cdot \frac{R}{r} \cdot e^{-\mu(r-R)}$$

The initial heating rate is related to the absorbed acoustic power as:

$$\left[\frac{\partial \tau}{\partial t} \right]_{t=0} = \frac{\langle g(r) \rangle_z}{\rho_L c_{mL}}$$

The steady-state ETCE for the array of N IUWAs can be written as:

$$\frac{\partial^2 \tau}{\partial x^2} + \frac{\partial^2 \tau}{\partial y^2} + \frac{\sum_{i=1}^N \langle g_i \rangle_z}{k_{eff}} = 0$$

4. ACOUSTIC PRESSURE AND INTENSITY RESULTS

4.1 Experimental set-up

The acoustic pressure due to interstitial ultrasonic waveguide applicators (IUWA) has been measured in water at room temperature. A block diagram of the set-up in fig.16 shows the components and the three functional sections used for pressure measurements.

Figure 16: Set-up for pressure measurements; three separate sections are indicated: power, detection and scanning.

The translational 2-D driving system was controlled by two indexers "Superior Electric" model SLO-SYN 430-PI. Each of the indexers could be addressed alternately through the same RS-232 port. Usually the applicator position was fixed and immersed in a water tank while the hydrophone was scanning the field either axially (in the z direction) or radially (in the r direction, away from the needle).

As detectors of the acoustic pressure, "Dapco Industries" miniature needle-like

ceramic hydrophones were used. The hydrophones were of 0.6 mm diameter and their signal was fed to the "Hewlett-Packard" spectrum analyzer (model 8553B for RF section, 8552B for IF section, and 141T for Display section). The peak detector of the spectrum analyzer was used to monitor the hydrophone signal. The analyzer's output was proportional to the vertical deflection of the spectrum analyzer display section and this output was recorded by the Data Acquisition System (DAQ in fig.16). DAQ consisted of Datascan-7010 and Datascan-7020 16-channels 32-bits modules and was RS-232 compatible.

The CW RF sinusoidal voltage controlling the IUWA was produced by the 3336C "Hewlett-Packard" synthesizer/level generator. It was operated around 1 MHz. It was provided with IEEE interface for reading and output control. During this study I performed tests with computer controlled frequency and amplitude, but in majority of measurements the output was set manually. Synthesizer signal after amplification by the "ENI" AP400B power amplifier was applied to IUWA piezoelectric. The amplifier could display approximate total and load power at the transducer. Precise reading of the rms signal amplitude was done with the "Fluke" 8920A digital voltmeter (DVM). DVM gives the true rms voltage on piezoelectric for frequencies up to 2 MHz. This device connected to the "Fluke" 1120A IEEE-488 translator can be addressed via GPIB port.

The data acquisition and scanning were PC controlled. I used the ³YST operating system well suited for communications and handling data. Ports COM1 and COM2 of the PC were devoted to DAQ and to indexers, respectively. The "National Instruments" IEEE-488 card supported communications with GPIB-addressable synthesizer

should be along a constant radial direction over several centimetres; otherwise results will show artifacts. Other experimental variables as driver vibrations or defects of the needle surface may influence the results, explaining the drop around 15 mm in fig.18. The decrease of the observed acoustic pressure supports theoretical prediction within about 15% of the 0.5 exponent.

Figure 18: Radial pressure in water

Beside this $r^{-1/2}$ radial dependence of pressure, a decrease in pressure due to radial attenuation is described by the amplitude attenuation coefficient $\mu/2$. Its reciprocal characterizes the distance over which the pressure amplitude decreases by e . Assuming $\mu \approx a$ as given in the Table 3, the pressure amplitude decreases 2.7 times over about 15 cm in both water and Aquasonic gel. Fig.18 suggests that the $r^{-1/2}$ dependence is the dominant one.

4.3.1 Axial periodicity of pressure patterns

All measurements of the pressure signal along the antenna were done at $r = 2.04$ mm from the needle. The hydrophone motion must be parallel to the applicator's antenna, which was an experimental challenge. Both cladded and uncladded applicators (in the latter case the immersed part of the needle serving as US source) were axially scanned for lengths ranging from 9 mm up to 25 mm. Even with good alignment (figs.19 and 20)

it is hard to say if a second mode of lower axial constant is present. This mode would be imbedded within the main one and it should have lower amplitude. Similar patterns have been observed for both clad and unclad applicators yielding the same axial periodicity constant Δ given in the Table 5.

Figure 19: Axial pressure pattern (unclad needle)

Figure 20: Axial pressure pattern (clad needle)

Fig.19 shows the acoustic signal along the antenna of an unclad 4-stage applicator operated at 0.97 MHz and 5V rms. Fig.20 presents similar data along the antenna of a 6-stage clad applicator operated at 1 MHz and 5V rms. The different acoustic transformers do not influence the axial periodicity constant close to 2.4 mm. In all these figures errors on position and measured signal are too small to be showed.

4.3.2 Intensity attenuation along the antenna

As it was mentioned before, the hydrophone signal squared will be proportional to the acoustic intensity. Following the axial pressure patterns described in figs.19 and 20, axial intensity at a fixed r was fitted according to the formula:

$$I(z) = A \cdot e^{-\nu z} \cdot \sin^2\left(\pi \frac{z}{\Delta} + D\right) \quad (35)$$

Eq.(35) is a modification of eq.(27) useful in a fit of experimental data. The term $\sin^2(2\pi z/\delta_0)$ in (27) has been changed to $\sin^2(\pi z/\Delta + D)$ due to the square of the signal, and a variable phase shift D added. The constant A characterizes total intensity at the fixed r under consideration.

Δ and ν were found using the Gauss-Newton method of curve fitting in a program written in ASYST. Figure 21 shows experimental results and curve fit for a 6-stages, 1 MHz, 5 V rms unclad applicator. The fit values were: $A=3.37 \text{ mV}^2$, $\Delta=2.34 \text{ mm}$, $\nu=0.0022 \text{ mm}^{-1}$ and $D=-0.05 \text{ rad}$. Signal irregularities are due to the misalignment or imperfections on the antenna radiating surface.

Acoustic pressure can be positive or negative reflecting local compression or dilatation of the medium, while detected signal is always positive. Because of that, both the hydrophone signal or the signal squared (proportional to intensity) can be used to get the axial parameters Δ and ν .

Figure 21: Experimental results and curve fit for absolute signal

4.3.3 Axial periodicity constant Δ

Analysis of axial intensity has shown that the acoustic transformer or the cladding doesn't influence the axial periodicity. The described fitting procedure has been repeated

for applicators with the same piezoelectric, but with different acoustic transformers of 2 to 6 stages. One applicator of each type has been scanned several times; results are not statistically significant from this standpoint. Results presented in the Table 5 suggest that Δ has an experimental value very close to the one predicted by the theory, $\Delta = 2.4$ cm (Table 3, mode $n=1$). In each case the value of Δ is clearly within one standard deviation of the theoretical Δ . The number of axial scans analyzed in each case was 17 for 3-stage, 30 for 5-stage and 25 for the 6-stage applicators. v in the Table 5 were obtained from 5 measurements for 3-stages and 15 measurements for 6-stages applicators. They were less precise and they indicate that the v value was small. Throughout this study v was assumed to be zero.

Table 5: Axial fit coefficients for 3, 5 and 6 stages transformer applicators.

# of stages	Δ (mm)	v (cm ⁻¹)
3	2.38 ± 0.04	-0.1 ± 0.1
5	2.50 ± 0.20	N/A
6	2.38 ± 0.06	-0.1 ± 0.2

4.3.4 Comparison of clad and unclad applicator

Fig.20 shows that the first two peaks are smaller than the third. This has been related to damping of vibrations by the cladding attached at the needle surface. Although cladding ring is supposed to fall on a node of vibrations, its finite thickness will reduce the wave intensity. For a skilful cladding installation the intensity was estimated to

correspond to $\sim 90\%$ of the unclad needle. Fig.22 presents pressure distribution along the 16.8 mm length antenna of a 6-stages applicator operated at 1 MHz and 5V rms. The ratio of clad over unclad applicator signal squared in this case is 0.87.

4.4 Antenna- medium interaction

In summary of experimental results for axial and radial directions, eq.(27) for local intensity can be re-written as:

$$I(r, z) = I(R, z) \frac{R}{r} \quad (36)$$

The axial attenuation was ignored and the radial attenuation was assumed negligible for regions not very far from needle where divergence prevails at low μ . The local intensity at the antenna surface, $I(R, z)$, is proportional to the acoustic pressure squared at that point, p_o . The pressure at the antenna surface can be correlated to

Figure 22: Comparison of unclad/clad signals

Figure 23: Pressure, intensity and source term

the acoustic loading ([8] pp.168-173) proportional to ρ_L and v_L . Therefore loading in air will be several orders of magnitude smaller than in water or Aquasonic gel. Change in magnitudes of the acoustic pressures in fig.23 was exaggerated to illustrate this effect. In

this approximation, pressure and intensity fields in the last two media will be about equal. In fig.23, at the antenna surface they were represented by the large peaks p_o and I_R , respectively; smaller values, due to the radial decrease, were $p(r,z)$ and $I(r,z)$. The radial decrease in pressure is not as rapid as the decrease in intensity.

Heat generated within a unit volume (or 'local source term') can be defined similarly to eqs.(29) and (30). It depends on the absorption coefficient of the medium and the local intensity at that point. Water has the absorption coefficient about 100 times smaller than brain tissue *in vitro*, which was assumed to be close to that of Aquasonic gel. Therefore for the same intensity at a point the absorbed heat will be different for water and gel phantom. In fig.23, g_R and $g(r,z)$ describe the local source terms at the antenna surface or within the phantom, but for Aquasonic gel only. Medium absorption can be related to its viscosity, heat conduction and other molecular properties [36].

4.5 Radiated energy for various acoustic transformers

In order to have a larger heated volume, it is important to get the maximum output intensity from each applicator. This depends on how well the operating frequency is determined but also on the efficiency of each acoustic transformer to convert bulk modes into surface waves. As it was presented in section 3.8, the local intensity integrated over the antenna's length (II) was used as a measure of the radiated energy. This quantity increased with the number of stages of the acoustic transformer. The first two columns in the Table 6 refer to the acoustic transformer design and give the number of stages and the transformer length. The quantity in the last column is proportional to the radiated energy across the cylindrical surface at $r = 2.04$ mm from antenna surface. The number

of stages is secondary because distal stages don't participate too much in mode conversion. Depending on the transformer design the angle of incidence of bulk waves will vary. This influences the conversion efficiency and the applicator output.

Table 6: Integrated intensity (II) for several acoustic transformers designs.

#stages	Transformer length [mm]	II
3	17.1	13.1±1.6
5	26.7	17.5±1.8
6	33.4	20.8±1.8

Evaluation of II (in arbitrary units) was done for antenna lengths varying from 10 to 24 mm. Integration was done for 14 scans of 3-stages applicator, 18 of 5-stages, and 16 of 6-stages applicator respectively. The results for II indicate that the radiated energy does not change much with the antenna length. However, the average intensity defined in section 3.8, $\langle I_r \rangle$, decreases with an increase of the antenna length and therefore of the lateral surface through which this energy is emitted.

All the above results were found at 5 V rms at the piezoelectric disc. At higher voltages (up to 30 V rms) 5-stages applicator had a better energy output than 6-stages. For this reason the applicators used in the array were mostly of 5-stages type.

4.6 Applicator output dependence on frequency

Each applicator has its best output at the operating frequency (OF). The OF depends on the manufacturing of the applicator. OF changes in time during the heating

process, initially very fast and stabilizing after several minutes. For several applicators with different OF but controlled from a single synthesizer, a difference between synthesizer's frequency (SF) and applicators different OF will appear. As OFs have narrow bandwidths, difference between SF and OF larger than few hundred Hz requires a tuning circuit attached to each of the applicators. The problem is also complicated by the applicator response in time to self-heating: it overheats if the applied SF is very different than OF and the applicator output decreases.

4.7 Tuning and matching in an IUWA array

Trials have been done to drive several IUWAs by a single synthesizer- power amplifier system. Fig.24 presents the set-up of the power control via a four-way split at the amplifier output. For these trials I used several tuning circuits (inductive and/or

Figure 24: Set-up for the four IUWAs array

capacitive) to pull-up or down the resonant frequency of each individual applicator. In the 3 applicators with 3 synthesizer-amplifier systems experiment the OFs were around 0.942 MHz, 1.005 MHz and 1.016 MHz, and they had to become compatible with a single SF. Beside tuning frequencies, a small resistance added into the circuit was used to set applicators output to a comparable value. Inductors of variable inductance L and/or capacitors of variable capacitance C have been mounted on a breadboard and connected to the IUWA piezoelectrics with wires soldered to the coaxial power cable inside the housing. Inductances in the 2 - 120 μH range and capacitances in the 3 pF - 10 pF range

have been used at about 1 MHz. With the capacitor in parallel, a decrease of the voltage across the piezoelectric plate was observed but the OF alteration was insignificant. Same small changes in OF (less than 1 kHz) were noticed when the capacitor was in series. With inductor in series, maximum changes in OF by 3-4 kHz were observed for $L \approx 120$ μH . However, the acoustic output as indicated by the hydrophone signal decreased by a factor of 1.5 - 2. Figs. 25 and 26 show some experimental results for series tuning inductance obtained for blue flag applicator at about 10 V rms.

Figure 25: Tuning with inductance in series

Figure 26: Resulting signal decrease

These results seem to take into account the difference between the electroacoustic system of IUWA (comprising the amplifier output, the tuning circuit, the piezoelectric disk and the region where the bulk waves propagate) and the purely acoustic system (the part of acoustic transformer and the waveguide where surface waves are present). Both of them are presented in fig.27. Tuning circuits produce an alteration of the resonant frequency of the electroacoustic system. However this change may be not strongly reflected in an alteration of the operating frequency. As OF was defined by maximum acoustic output into the medium, parameters related the surface mode (conversion

efficiency, surface defects) seem to prevail over those related to the initial bulk wave in establishing this OF.

Heating results described in the following section were obtained with up to four IUWAs. They were controlled by up to three synthesizer-power amplifier systems. This way, not only the tuning to OFs but also the delicate problem of matching their individual signal outputs to a common value

Figure 27: Electro-acoustic and mechanic components of IUWA

was partly skipped. It is believed that in the long run (with a significant pool of applicators built in a more standardized way) this 'splitting power from a single source' approach may succeed.

5. HYPERTHERMIA EXPERIMENTS

The time dependence of temperature elevations for a single IUWA applicator have been discussed before ([2], [3]). Temperature patterns detected at 2 mm away from a 15 mm long antenna, were similar for a small and a large tissue sample *in vitro* [2]. In this chapter temperature distributions in similar or larger volumes of Aquasonic gel phantom will be presented for an array of several applicators.

5.1 Experimental set-up

For temperature measurements the pressure set-up presented in fig. 16 was modified and some components replaced.

5.1.1 General set-up

Figure 28: Experimental set-up for temperature measurements

Fig.28 illustrates the general set-up for phantom hyperthermia experiments. It consists of

the power section (synthesizer, power amplifier and DVM) and the detection section (thermistors and data acquisition system, DAQ) as in section 4.1. In some cases a hydrophone was used in the set-up to choose proper operating frequency of the applicator.

5.1.2 Phantoms

Hyperthermia phantoms were made of Parker Labs Aquasonic 100 gel. In the technical data sheet, the gel was described as an aqueous gel of density 1.08 g/cm^3 and sound propagation velocity of 1490 m/s . These values are close to those for water but the gel was a very viscous medium. The gel was placed in specially designed plastic containers. Several such units (they will be called V#1, V#2, etc) have been used during this study. V#1 was a cylindrical plastic vial and was previously used in the lab with a single applicator. It was 26 mm in diameter with 1.6 mm thick walls. The plexiglass container V#2 was used with 1 and 2 applicators. It had 40 mm length, 20 mm width and 15 mm height. Container V#3 was of the same shape, $40 \times 20 \times 25 \text{ mm}^3$, and both of them had about 3 mm thick walls. V#4 was a plexiglass cylinder and was used with up to four applicators. It had 87 mm diameter, 40 mm height and its wall had 7 mm thickness. All the container heights (except V#2) were larger than the antenna length. The respective volumes of V#1 to V#4 were: $V_1 \approx 8 \text{ cm}^3$, $V_2 = 12 \text{ cm}^3$, $V_3 = 20 \text{ cm}^3$ and $V_4 = 238 \text{ cm}^3$.

All containers had pre-drilled holes to hold Fenwal Electronics microthermistors in fixed positions. The microthermistors had less than 0.3 mm sensitive beads and they were connected by thin wires of less than $30 \text{ }\mu\text{m}$ diameter to an external resistance bridge. The small bead size insures that no significant heating takes place within the thermistors body placed far from the antenna. All thermistors have been calibrated against a YSI

44201 thermolinear thermistor. A small empirical offset has been applied after calibration to make them all indicate the same temperature under the same condition. In the following, micro-thermistors will be addressed as T#1, etc.

All the heating experiments were 2-D problems, considering the temperature elevations along the antenna about constant [1]. Generally thermistors were located in the median plane of the antennas. The thick walls of some containers (e.g. V#4) were thermally insulating the gel phantom. When several applicators were used, they were flagged with different colours and they will be addressed as 'the white flag applicator' (WF), etc.

5.2 Hyperthermia with single IUWA

Measurements were carried out using one, two, three and four IUWA arrays under conditions specified for each case.

Fig.29 a) shows several common features of a single IUWA heating curve. US power was turned on at about 5 min. Initially the rms voltage at the applicator's transducer was 27 V and the frequency was 0.9965 MHz. During the first stage of increase in temperature, the frequency was adjusted within 0.9965 - 0.9945 range. Eventually the temperature reached a constant temperature elevation (plateau). In all measurements presented in this chapter, the plateau of temperature elevation was achieved by reducing the applied voltage. The plateau in fig.29 a) was obtained with the rms voltage maintained at 23 V and the frequency at 0.996 MHz. The arrow indicates the plateau time constant Δt_p defined in section 3.11. For a good heating it should be as small as possible. The plateau can be sustained for a very long time.

Figure 29: a) Heating curve for dark flag (DF) applicator in $4 \times 2 \times 1.5 \text{ cm}^3$ phantom (V#2); b) cross-section of the experimental set-up with thermistors approximately at the centre of the circles.

Temperature elevations were measured at distances varying from 4 to 25 mm from the antenna as shown in fig.29 b). There was no difference between temperature elevation detected by T4 and T5 to the right and the left of the applicator. Thermistors #2 and #3 shown unexpectedly close temperature elevations. Inhomogeneities within the gel (e.g. small air bubbles) were most likely responsible for these temperature fluctuations. Also the precision in positioning the thermistors (of about ± 1 mm) influenced temperature results. This error was mainly due to the wire bending within the gel and the bead orientation. All five temperature elevations reached their plateau although there was a time delay for farthest locations.

5.3 Hyperthermia with an array of two IUWAs

The heating curve in fig.29 a) can be compared to fig.30 a) which shows heating curves for dark flag (DF) and white flag (WF) applicators controlled from a single synthesizer-power amplifier system. OFs around 0.996 MHz and around 1.002 MHz for DF and WF, respectively, were determined prior to the experiment at 27 V rms. The synthesizer frequency was varied from 0.997 to 0.992 MHz while the measured voltage across each applicator was between 23.5 to 28 V rms. The plateau was achieved at 0.9935 MHz and 23 V rms. Thermistors positioning is presented in fig.30 b).

None of the applicators had tuning or matching circuits. Hydrophones close to each applicator indicated that the WF was radiating more power than DF despite the fact that the synthesizer frequency was kept closer to the OF of the DF applicator. This unbalanced power output of the two applicators explains the temperature elevation succession $\tau_2 > \tau_1 = \tau_4 > \tau_3 > \tau_5$ observed in fig.30 a). The plateau of temperature

Figure 30: a) Heating curves for white flag (WF) and dark flag (DF) applicators in the $4 \times 2 \times 1.5 \text{ cm}^3$ container (V#2); b) cross-section diagram showing applicator locations and thermistors.

Figure 31: a) Heating curves for yellow flag (YF) applicator in 87 mm radius Aquasonic gel phantom at around 1.01 MHz and 12.5 V rms; b) Distribution of final temperatures; c) Cross-section of phantom showing thermistor positions with respect to the applicator: $r_{T1} = r_{T2} = 40$ mm; $r_{T3} = 57$ mm; $r_{T4} = 4$ mm; $r_{T6} = 60$ mm; $r_{T7} = 21$ mm; $r_{T8} = 36$ mm; $r_{T9} = 26$ mm; $r_{T10} = 12$ mm; $r_{T11} = 19$ mm.

elevations were different at right and left of each needle and they varied from one applicator to the other. The five plateau values are higher and closer to each other for the array than for a single applicator. Also, the delays these plateau were produced at various locations decreased in the case of array. All these indicate the array generated more heat within the phantom with a more uniform temperature distribution.

5.4 Temperature distribution analysis for a single IUWA

For passive heating with a single needle the temperature decreases logarithmically with the radial distance (see Appendix 1). A single cylindrical source produces temperature distribution dependent on the phantom conductivity coefficient k , unknown for the Aquasonic gel.

Fig. 31 a) shows heating curves for the single yellow flag (YF) applicator in the large cylindrical Aquasonic gel phantom of 87 mm radius (V#4). The frequency was maintained in the 1.010 - 1.004 MHz range with the rms voltage of 12.5 V. IHR for each thermistor has been found from the initial linear part of these heating curves. Eq.(31) gives a linear relationship of IHR vs. $1/r$. Plotting measured IHRs at different thermistor locations, the slope of this relationship has been found as:

$$\frac{g_o}{c} = \frac{\rho}{R} \text{slope} = \frac{1.05}{0.55} (0.496 \frac{^{\circ}\text{C}\cdot\text{mm}}{\text{min}}) = 0.0158 \frac{\text{W}/\text{cm}^3}{\text{J}/\text{g}^{\circ}\text{C}} \quad (36)$$

with $\rho=1.05 \text{ g/cm}^3$ and $R=0.55 \text{ mm}$. The above expression relates the source term on the needle, g_o , with the specific heat capacity of the Aquasonic gel, c .

The heating was delivered for about 4 hours. Fig.31 b) presents the maximum temperature distribution at different distances r from the antenna. Experimental error on

temperatures was considered to be $\pm 0.1^\circ\text{C}$, which was deduced from the indications of symmetric thermistors T1 and T2. The fit of the data was a logarithmic dependence of plateau temperature elevation with distance and it is shown by the solid line in fig.31 b). The extrapolation of this fit line at $r = R = 0.55$ mm gives the temperature on the needle, $\tau_i = 7.31^\circ\text{C}$. Thermistors covered the range 4 - 60 mm described in fig.31 c). The outer boundary was expanded to $r = 110$ mm away from the needle to take the wall thickness into account. The temperature elevation at this distance was $\tau_o = 1.74^\circ\text{C}$.

The fit curve from fig.31 b) extrapolated over the 0.55 - 110 mm range was compared in fig.32 with simulated results for a similar phantom. Details of simulations will be discussed in chapter 6. τ_i and τ_o

had the values specified above. Pairs of values (g_o , c) satisfying eq.(36) with $c = 4$ J/g $^\circ\text{C}$ suggested that the source term should be less than 0.07 W/cm 3 which corresponded to a low voltage used. Under these conditions, the values in 0.004 - 0.03 W/cm $^\circ\text{C}$ range for k were assumed (given in fig.32) and each

Figure 32: Experimental/simulation fit for Aquasonic gel phantom

resulting simulated temperature distribution was compared to the experimental fit in fig.31 b) at the location of each of the thermistors. Solid simulated temperature distribution matched the best the experimental points with a large k used. The matching was more sensitive to the conduction coefficient k variations than to specific heat c . The best fit was

Figure 33: a) Heating curves for three IUWAs in cylindrical 87 mm radius Aquasonic phantom (V#4); b) Cross-section showing thermistors and white (WF), yellow (YF) and blue (BF) flag applicators. Distances are: $r_{T1-BF}=r_{T2-WF}=5$ mm; $r_{T3-YF}=4$ mm; T8 at the centre; $r_{T4-T8}=r_{T6-T8}=20$ mm; $r_{T5-T8}=40$ mm; $r_{T7-T8}=12$ mm; $r_{T9-T8}=33$ mm; $r_{T10-T8}=25$ mm.

obtained for $g_0 = 0.066 \text{ W/cm}^3$, $c = 4.2 \text{ J/g}^\circ\text{C}$ and $k = 0.03 \text{ W/cm}^\circ\text{C} = 3 \text{ W/m}^\circ\text{C}$. This suggested the conduction coefficient of Aquasonic gel is about an order of magnitude larger than the value for brain *in vitro*. This can make the phantom equivalent to brain *in vivo* where the blood flow leads to an increase of tissue effective thermal conduction coefficient. In all simulations I considered the decrease in ultrasound power absorption (source term) affected only by divergence. For non-negligible attenuation term, a decrease in the source term can be compensated by similar small decrease in k . Therefore, in the final simulations for Aquasonic gel the value $k=0.025 \text{ W/cm}^\circ\text{C}$ has been used.

5.5 Hyperthermia with an array of three IUWAs

Fig.33 a) shows the heating curves in Aquasonic gel cylindrical phantom of 87 mm radius. The three applicators (BF, YF and WF) were driven by three individual synthesizers-power amplifier systems. The OFs of each applicator were determined prior to the experiment and they were around 0.942 MHz at 27 V rms for BF, 1.005 MHz at 21 V rms for WF and 1.002 MHz at 18 V rms for YF.

Thermistors locations are indicated in fig.33 b). Temperature elevations next to the needles are indicated by thermistors T1, T2 and T3. The evolution in time of these three temperatures is very similar indicating balanced power outputs from the three antennas. This well controlled heating process was made possible by the individual synthesizer-power amplifier systems operated at OF and with adjustable power outputs. The 5.9°C plateau of temperature elevation next to needles has been reached in less than $\Delta t_p = 100$ min. Due to the high conductivity of the medium and insulating properties of the container walls, temperature elevation of $6-3.5^\circ\text{C}$ over the whole sample volume was achieved.

Figure 34: a) Heating curves for four applicators in the cylindrical Aquasonic phantom of 87 mm radius (V#4); b) Cross-section showing same applicators as in fig.33 plus the red flag applicator (RF). The only changed thermistor distances are $r_{T4,RF} = 4\text{mm}$ and $r_{T9,RF} = 14\text{ mm}$, others are as in fig.33 b).

5.6 Hyperthermia with an array of four IUWAs

Fig.34 a) presents the heating curves for an array of four applicators (black (BF), yellow (YF), white (WF) and red (RF) flags) in the 87 mm radius phantom of Aquasonic gel. The applicators were controlled by three synthesizer-power amplifier systems. The YF and WF applicators were controlled by a common system. Initially YF ran alone at about 1.016 MHz and after about 8 min WF applicator was connected and synthesizer frequency changed to 1.004 MHz. Rms voltage at the YF applicator was about 13 V and it was about 18.5 V at the WF applicator. A 14.2 μ H inductor in parallel with 3 nF capacitor was connected in series with the WF applicator; a 1.5 μ H inductor was connected in series with YF. These circuits were used for matching the YF and WF applicator outputs, but the outputs depended also on how close the synthesizer frequency was to applicators' OF. The continuous toggling of synthesizer frequency between the two different OF can be noticed in T2 and T3 heating curves, for locations showed in fig.34b). The other two applicators were individually controlled. BF IUWA was operated at 0.942 MHz and 22.5 V rms, while RF IUWA was operated at 0.938 MHz and 22.5 V rms.

The levelling of the four applicators array had to be done at the level of the weakest one and this decreased the overall heating efficiency of the system. Fig.34 a) shows reasonable differences between patterns recorded next to each needle by T1, T2, T3 and T4 thermistors. BF applicator had a higher P_{oi} than any of the other three applicators which operated at low P_{oi} . Therefore the RF electric power supplied to BF was gradually reduced. This resulted in an increased plateau time constant Δt_p . The 6°C plateau temperature elevation was reached after around 180 min.

As monitoring thermistors were placed at 4-5 mm distance from the applicators, the temperature on the antennas' surface must have been higher than 6°C, likely in the 6.5-7.5 °C range.

5.7 Special aspects of hyperthermia produced with IUWA

5.7.1 Power estimations at the needle surface

Replacing the expression (29') (with the attenuation term neglected) in eq.(31), the initial heating rate (IHR) at a distance r , this distance and the source term at the antenna surface g_o were related by:

$$g_o = \rho c \left[\frac{\partial \tau}{\partial t} \right]_{r=0} \frac{r}{R} \quad (37)$$

where ρ is the density and c is the mass specific heat of the medium. For Aquasonic gel and brain, the product ρc lies within the 3-5 J/cm³°C range.

Typical values of IHR for a single IUWA radiating in the V#3 and V#4 gel phantoms were at least 0.2 °C/min. This was the value recorded by the closest-to-antenna thermistor at the distance $r = 4 \pm 1$ mm from the needle. The precision of the microthermistor position was limited essentially by the bead positioning, bending of thermistor wires during installation, etc. The resulting source term on the needle, g_o , was calculated with (37). In the estimation presented in the Table 7, the absorption coefficient $a = 0.1 - 0.3$ cm⁻¹ was used. Based on the value found for g_o , the intensity at the surface of the needle, I_o , and the power radiated through this surface, P_o , were calculated for $R=0.055$ cm radius and $L_o=1.5$ cm length (antenna's lateral surface was 0.52 cm²). Maximum, minimum and most probable estimates for single IUWA at high voltage are

showed in Table 7:

Table 7: Estimates of IUWA power output based on IHR measurements of $0.2^{\circ}\text{C}/\text{min}$

	a cm^{-1}	r cm	ρc $\text{J/g}^{\circ}\text{C}$	g_o W/cm^3	I_o W/cm^2	P_o W
min	0.1	.3	3	0.050	0.200	0.1
Max	0.3	.5	5	0.150	1.500	0.8
probable	?	.4	4	0.100	0.700	0.5

For some applicators, values larger than $0.2^{\circ}\text{C}/\text{min}$ have been observed. Still, compared with the observed forward power this means that only 5 to 10 % of the total electric power was used in the acoustic output. The values in the last row of the table 7 (probable) were used in the simulations (ch.6).

In the terminology introduced in section 3.11, the values of P_o designate the initial average power at antenna surface P_{oi} (used for temperature increase region). For the experiment presented in fig.33 a), eq.(34) was used to estimate IUWAs' average performance. With $\Delta t_p \approx 100$ min, $V = 240 \text{ cm}^3$, $\rho = 1.05 \text{ g/cm}^3$, $c_m = 4.2 \text{ J/g}^{\circ}\text{C}$ and an estimated average temperature increase over the whole volume $\tau_s = 4^{\circ}\text{C}$, the average power for each of the three IUWA was found to be $P_{of} = 0.240 \text{ W}$; same calculation for $\tau_s = 4.5^{\circ}\text{C}$ yielded 0.260 W . In the case of four IUWAs array described in fig.34 a), the value of $\Delta t_p \approx 200$ min gives $P_{of} = 0.100 \text{ W}$ assuming $\tau_s = 4.5^{\circ}\text{C}$, and 0.110 W if $\tau_s = 5^{\circ}\text{C}$. Differences in estimated powers between these two cases showed the importance of

operating each of the IUWA in the array at its OF. This resulted in higher P_{of} , smaller Δt_p and eventually higher P_{of} on each of the applicators. All these values depended on the volume of the phantom V.

5.7.2 Heating for various antenna lengths

The dependence of the average power (and therefore of the source term and IHR) on antenna length L has been verified for a 5-stage applicator in V#2 Aquasonic gel phantom. Figure 35 shows the initial heating curves at 27 V rms and 1.002 MHz. Lines without symbols

Figure 35: IHR for two antenna lengths at three positions.

describe heating produced by the antenna length $L_1=12$ mm at three different thermistor locations. Solid lines are at 5 mm right, long dashed lines are at 5 mm left and short dashed are at 13 mm left of the applicator. The similar type of line with dots describe the heating generated by $L_2=20$ mm antenna at the same locations. With the same power coming out from the antenna, P_o , the ratio IHR_1/IHR_2 can be calculated from eqs.(27) and (31) as $L_2/L_1=1.67$. The experimental values for the three locations were found to be 1.63, 1.81 and 1.53, respectively. Their average value was 1.66 ± 0.14 , and fluctuations can be explained by the limited precision in thermistor locations.

5.7.3 Heating dependence on frequency

As mentioned in section 4.5, heating efficiency depended on how close the

operating frequency (OF) of each applicator and the synthesizer frequency (SF) were to each other. Losing OF during the heating process transforms that IUWA from a source into a sink of energy and consequently temperature around that needle may even decrease. A lost OF is signalled by a reduction in the rate of temperature increase and the re-adjusted synthesizer frequency boosts up the rate of temperature increase. If such corrections don't produce any observable rate increase, it is likely the applicator approaches its limit with the overheated piezoelectric producing a decreased output. As mentioned in section 3.11, thermal plateau obtained by lowering down the voltage created a forced thermal equilibrium within the medium, at which the outer boundary regions reacted with a delay. This suggested that if more time were allowed, the outer boundary temperature τ_o would be lower.

In experiments performed in this study, the OF was pre-determined and during the heating process SF tried to approximate this value as close as possible. There were two different ways to adjust frequency such that the acoustic output was maximum. Fig.36 shows

Figure 36: Continuous OF adjustment (dashed line) vs. fixed OF (solid line) methods

the two heating curves for the 5-stages white flag applicator operated around 20.5 V and 1.005 MHz in V#4 Aquasonic gel phantom. The thermistors were supplemented by a monitoring hydrophone in the experimental set-up. The dashed line was obtained by continuously adjusting SF such that the hydrophone signal was maximal. This insured that SF corresponded to OF throughout the experiment. The initial value of frequency was about 1.009 MHz and it was decreasing very fast. At the end of the heating interval of time of 13 min it has almost stabilized at around 1.005 MHz. This final frequency value was set on the synthesizer at the beginning of the fixed OF method experiment (the solid line) and kept constant over the whole measurement period.

The continuous adjustment method insures IUWA to be at OF at every moment but the use of the hydrophone makes it impractical. The fixed frequency method is much simpler requiring only a prior determination of OF value for a given voltage. Fig.36 indicates a time delay of about 2 min between the fixed and continuous adjustment methods. Fixed OF method assumes the existence of an unique OF at a given voltage. During my measurements some applicators behaved this way, e.g. BF operated at unchanged frequency of 0.942 MHz and 27 V rms over several hours. Other applicators (YF, WF) operated at high voltages required small frequency adjustments from time to time in order to avoid losing OF.

5.8 Conclusions of hyperthermia measurements

Hyperthermia measurements were done with up to four IUWA applicators. The phantom used was made of Aquasonic gel and had 8.7 cm radius and 4 cm height with a total volume of about 240 cm³. The antennas were 1.5 cm long.

Heating characteristics were better (e.g. similar temperature elevation achieved in a shorter interval of time) when applicator operating frequencies (OFs) corresponded closely to the synthesizer frequency (SF). The array of three IUWAs produced temperature elevation of about 6°C in 100 min at distances of 4-5 mm from each antenna (fig.33 a)). About the same temperature elevation at similar distances was obtained with four applicators (fig.34 a)). The last array was controlled by three synthesizer-amplifier systems. Plateau temperatures were achieved in about 200 min.

Heating results supported the inverse proportionality of the antenna average intensity with its length. Typical antenna initial outputs encountered at high voltages (up to 30 V rms on IUWA piezoelectric) were estimated in the Table 7. Probable values for 1.5 cm long, 0.055 cm radius single IUWA were: the average intensity on the needle of 0.7 W/cm²; the total acoustic power 0.5 W; and the source term on the needle $g_0 = 0.100$ W/cm³. For an array of IUWAs, the phantom average temperature elevation depended on the volume of phantom considered, on the time this plateau was achieved, and on the number of applicators in the array.

For a single IUWA the temperature elevations were measured over large distances (4 - 60 mm). The temperature elevation followed a logarithmic decrease with distance from the needle. Comparison with simulated fields suggested that the phantom used had high conduction coefficient of around 0.025 W/cm°C. This is several times higher than thermal conduction coefficient for brain tissue *in vitro*, but possibly similar to that for brain *in vivo* in the presence of blood flow.

6.HYPERTHERMIA SIMULATIONS

Temperature measurements were performed at ten locations in the Aquasonic gel phantom. The discrete nature of temperature detection can not predict the temperature at every point in the phantom. In this chapter, 2-D steady-state simulations for various irradiation conditions will be presented. They were obtained using finite element analysis (FEA). Some of these simulations were compared with experimental results.

6.1 FEA simulations

Analytic solution of the effective thermal conductivity equation (ETCE) formulated in section 3.10 is very cumbersome for low symmetry problems. FEA approach is more effective and it was used in the following. Simulations were done using the thermal module of ALGOR, a commercially available FEA software. The whole phantom volume was discretized into small elements and will be referred to as 'the mesh'. Colour filters have been used for regions of special interest (internal and external boundaries, sources regions next to each needle). The final mesh was completed by initial and boundary temperature conditions. This model was constructed using SUPERDRAW II module and it was saved as a .esd file. The other main components used in thermal modelling with ALGOR are presented in fig.37. The figure doesn't include display and printing utilities because they varied during simulations.

The mesh was visually checked in the SUPERVIEW module and the non-intersecting lines were corrected in SUPERDRAW II. After this step an .svt file was created. The corrected mesh, subject to the specified boundary conditions, was pre-

Figure 37: The main components of ALGOR thermal modelling

processed by the THERMAL DECODER module, where thermal parameters (g for various layers, c , k , L) were added. The files produced at this stage had extensions .esg, .emt and .stt. The MATH PROCESSOR module processed the above files and created .do, .tso, .l, .log, and updated .stt. At this stage, the data was transferred to THERMAL SUPERVIEW module where final images of the temperature distribution were saved as .btm files.

In the models I generated, the maximum number of elements used was around 5000 nodes and 12000 lines. Their number was related to the geometry and tolerance used. All problems presented here had 2-D meshes corresponding to the median plane of the antennas. 'Acoustic gel phantom' refers to a low-conductivity medium ($0.0025 - 0.0045 \text{ W/cm}^\circ\text{C}$) similar to brain tissue *in vitro*, while 'Aquasonic gel phantom' refers to the gel phantom used.

6.2 Simulations for a single applicator

Figure 38 gives an illustration of the test problem solved in Appendix 1.

Figure 38: Temperature distribution for purely conductive test-problem.

For this simulation it was assumed that a 'hot' needle of radius $R=0.055$ cm is maintained at $\tau_i=10^\circ\text{C}$ at the centre of 1.3 cm radius phantom. A uniform conduction occurred with the temperature elevation of $\tau_o=0^\circ\text{C}$ on the outer boundary. Results of simulation in fig.38 assume no sources present, e.g. $g(r) \equiv 0$ everywhere. The hyperthermic range inside the green region was considered to be above 5°C . Its maximum value was at the needle surface. Within this circle of about 5 mm outer diameter temperature decreases from 10°C to 5°C .

As discussed in Appendix 1, the ordinary differential equation describing the temperature distribution as in fig.38 is k -independent and the steady-state solution depends only on the boundary temperatures. The nature of the phantom medium and its walls are indirectly present in how long it will take to reach this thermal equilibrium.

Figure 39: Hyperthermia simulations for single IUWA in the 2.6 cm diameter vial V#1: source term $g_s = 0.100 \text{ W/cm}^3$ and medium of low $k = 0.0025 \text{ W/cm}^\circ\text{C}$ were assumed; boundary temperatures: a) $\tau_i = 10^\circ\text{C}$, $\tau_o = 0^\circ\text{C}$; b) $\tau_i = 10^\circ\text{C}$, $\tau_o = 2^\circ\text{C}$.

The dependence of the hyperthermic range on the outer boundary temperature is presented in figs.39 a) and b). In both simulations a source term on the needle $g_o=0.100$ W/cm³ was assumed. The phantom geometry and the colour code used was the same as for fig.38. The conductivity of the medium was supposed to be $k=0.0025$ W/cm°C. Boundary temperatures in fig.39 a) were the same as in fig.38, i.e. $\tau_i=10^\circ\text{C}$ and $\tau_o=0^\circ\text{C}$. In fig.39 a) the hyperthermic region has about 7 mm diameter, just slightly larger than in fig.38, the conduction case. In fig.39 b) the outer temperature has been increased to $\tau_o=2^\circ\text{C}$ with other parameters unchanged. The hyperthermic region increased to about 10 mm diameter with this τ_o increased. In the presence of the sources, the temperature distribution depends also on the conduction coefficient. For a single IUWA it was verified that hyperthermic range decreases when k increases.

6.3 Four applicators at the corners of a square 36 mm on side

Fig.40 shows the mesh used in simulations for four applicators at the corners of a square of 36 mm on side. The scale for this mesh is different than for a single applicator and it is shown in fig.41. The figure presents the hyperthermia effects within a 8.7 cm radius acoustic phantom of low $k=0.0025$ W/cm°C in the absence of the source term. Each applicator was assumed to be at constant temperature, $\tau_i=10^\circ\text{C}$. The outer phantom boundary temperature was $\tau_o=0^\circ\text{C}$. Same mesh and colour code were used in figs.42 a) and b). In all these figures, the hyperthermic range 5°C - 10°C corresponded to the area within the green colour. The blue colour represented regions at lower temperatures. In fig.42 a) and b) the assumed source term was $g_o=0.1$ W/cm³ on each of the four needles.

Figure 40: Mesh used in simulation for 4 IUWAs at corners of a square 3.6 cm on side.

Figure 41: Hyperthermia simulations with 4 hot needles placed in the above geometry.

Figure 42: Hyperthermia simulations for four IUWAs at the corners of a square 3.6 cm on side; phantom geometry is shown in fig.40; boundary temperatures $\tau_i=10^\circ\text{C}$ and $\tau_o=0^\circ\text{C}$; $g_o=0.100\text{ W/cm}^3$; a) low $k=0.0025\text{ W/cm}^\circ\text{C}$; b) increased $k=0.0045\text{ W/cm}^\circ\text{C}$.

Figs.42 a) and b) show the dramatic difference between the active heating using heat sources and the passive one (just conduction, as in fig.41). In the latter case, the only way to increase the hyperthermic range for a given phantom and outer temperature τ_o is by increasing τ_i . In the former case, the range depends largely on the sources power of g_o , whose value of 0.100 W/cm^3 seems to be adequate to heat a large region. In fig.41 the hyperthermic range around each needle is almost circular with less than 1 cm diameter. As it was already pointed out in fig.32 for a single applicator, the conduction coefficient k has a strong influence on temperature distribution. Figs.42 a) and b) show how this distribution changes when k is almost doubled from $0.0025 \text{ W/cm}^\circ\text{C}$ as in fig.42 a) to $0.0045 \text{ W/cm}^\circ\text{C}$ in fig.42 b) with all other parameters unchanged. The increased k shrinks down the size of the hyperthermic range and the temperature in the inner region goes down as well. Ranges have a four-lobes shape with a maximum distance D between lobes and a minimum distance d occurring at middle (see fig.42 a)). For fig.42 a), these distances were $D = 5.5 \text{ cm}$ and $d = 5 \text{ cm}$, while in fig.42 b) they were measured as $D = 5 \text{ cm}$ and $d = 4 \text{ cm}$. Also, in fig.42 a) most of the inner region between needles was at around 7.5°C (red colour) while in fig.42 b) it was at around 6°C (green-blue). However, for higher k the temperature field inside the square delimited by the four applicators is more homogeneous than in the case of lower k .

6.4 Four applicators at the corners of a square 24 mm on side

During measurements in the high conductivity Aquasonic phantom with an array of four IUWAs, temperatures of less than 10°C were observed next to each applicator. Hyperthermic ranges of 5°C - 10°C with lower τ_i require a decrease of the distance

Figure 43: The 8.7 cm diameter mesh used for modelling four IUWAs located at the corners of a 2.4 cm side square.

Figure 44: Percentage source (with $g_0 = 0.100 \text{ W/cm}^3$) used for various layers around each needle.

100 mW/cm² sources, steady state
 $T_c/0.50$
 needles 24 mm apart

$k=0.0025$

a)

1 cm

$k=0.0045$

b)

Figure 45: Simulated hyperthermia for four needles at the corners of a 24 mm square: phantom geometry is described in fig.43, boundary temperatures were $\tau_i=7^\circ\text{C}$ and $\tau_o=0.5^\circ\text{C}$; a) low $k=0.0025\text{ W/cm}^\circ\text{C}$; b) increased $k=0.0045\text{ W/cm}^\circ\text{C}$.

between applicators. In this section, simulations were done with the four IUWAs placed at the corners of a square 24 mm on side. The same geometry was used for the experiments presented in section 5.6, with which these simulations may be compared.

The aspect of the mesh used changed and it is shown in fig.43. The same cylindrical phantom of 8.7 cm radius was considered. In simulations, the same source term at each IUWA was assumed, $g_0=0.100 \text{ W/cm}^3$. The way the decrease of each source term due to the divergence was implemented in the simulations is presented in fig.44. Here the respective percentages of g_0 were applied over the region of the assigned colour.

Figures 45 a) and b) complete the series of simulations for a low conductivity coefficient phantom (fig.41 and 42 a), b)). Hyperthermic range was kept unchanged, 5°C – 10°C , for the sake of comparison using the same colour code. In fig.45 a) and b) the temperature elevation at each antenna was assumed to be $\tau_i=7^\circ\text{C}$ and that at the outer boundary to be $\tau_o=0.5^\circ\text{C}$. However, the region between needles was in both cases at a temperature higher than τ_i . E.g the yellow region in fig.45 a) was at around 9°C and the red region in fig.45 b) was at about 7.5°C . This is correlated to the low conduction coefficient in both simulations, $0.0025 \text{ W/cm}^\circ\text{C}$ in fig.45 a) and $0.0045 \text{ W/cm}^\circ\text{C}$ in fig.45 b). Such central hot region was not observed in experiments in Aquasonic gel phantom, supporting the finding from section 5.4 that the medium used had a high thermal conductivity. For both bigger and smaller distances between applicators, the increased k produced a shrinkage of the hyperthermic region which in the case of figs.45 a) and b) changed from $D \approx d = 5 \text{ cm}$ to $D \approx d = 4 \text{ cm}$, respectively.

The three figures 46 a), b) and c) show hyperthermia simulations for a higher k

$k=0.025 \text{ W/cm}^\circ\text{C}$

needles 24 mm apart

a)**7.5/3 C** **b)****7/3 C**1 cm

Figure 46: Hyperthermia simulations for four IUWAs placed at the corners of the square 24 mm on side in the cylindrical Aquasonic gel phantom of 87 mm diameter and $k=0.025 \text{ W/cm}^\circ\text{C}$; a) $\tau_i=7.5^\circ\text{C}$ and $\tau_o=3^\circ\text{C}$; b) $\tau_i=7^\circ\text{C}$ and same outer temperature.

Figure 46 c) Same as before with $\tau_s = 6.5^\circ\text{C}$ and other parameters unchanged.

Figure 47: The above simulation with appropriate 6.5°C - 5.2°C temperature range.

(close to the predicted value for Aquasonic gel). In all the three cases, the conduction coefficient was $0.025 \text{ W/cm}^\circ\text{C}$ and the other common parameters used were $c = 4.2 \text{ J/g}^\circ\text{C}$ and $g_o = 0.100 \text{ W/cm}^2$. Experiments suggested a relatively high temperature elevation at the outer boundary and for simulations the value of $\tau_o = 3^\circ\text{C}$ was assumed. Temperature on the needle, τ_i , was chosen as 7.5°C in fig.46 a), 7°C in fig.46 b) and 6.5°C in fig.46 c). All these three values seem plausible from experimental standpoint. The size of the central region, d , measured from each figure was 48 mm, 43 mm and 37 mm, respectively. The temperature elevation of the central region dropped from around 6.7°C in fig.46 a), to 6.25°C in fig.46 b) and to 5.9°C in fig.46 c), when τ_i was reduced. The colour code used in this set of graphs does not correspond to the code used in figs.45 a) and b). However, these combined simulations indicate that for a given τ_o , an increased τ_i or a decreased k have similar effects, e.g. increased hyperthermic range and higher temperature elevation in the central region. Conversely, a higher conductivity or a lower temperature at the needle decreases the hyperthermic effects.

Fig.46 c) was re-drawn using the appropriate temperatures limits as fig.47. The new colour code described the hyperthermic range 5.2°C - 6.5°C . The inside red region of $D = 30 \text{ mm}$ and $d = 25 \text{ mm}$ had almost uniform temperature elevation of around 5.9°C . The surrounding, above 5.3°C , green square region was about 37 mm on side. Figure 48 is just an enlarged part of fig.47 around one of the applicators. It shows that the temperature elevation dropped from 6.5°C to about 5.9°C in the inward direction over a distance of around 4 mm and from 6.5°C close to 5.3°C over less than 6 mm outward. In each of the simulations presented in figs.45 and 46 one can distinguish three parts of

the hyperthermic range: one next to each applicator, a region between the four applicators which will be referred to as the inner region, and an external one.

Figure 48: Enlarged view of fig.47 showing fast drop in temperature around a IUWA.

6.5 Comparison of experimental hyperthermia with simulations

Figure 49 concludes the experimental and simulated results obtained with an array of four IUWA located at the corners of a square 24 mm on side and radiating into the Aquasonic gel phantom of 8.7 cm radius, V#4. For thermistor positioning the reader is referred to fig.34 b). Experimental bars represented the average plateau temperature elevations measured at each location with a precision of $\pm 0.1^{\circ}\text{C}$ indicated in fig.49 a). The difference (experimental-simulated temperature increase) was found for each thermistor and binned into a diagram. In calculating the average difference, all thermistors were

Figure 49: Comparison of experiments and simulations for cylindrical Aquasonic gel phantom of 8.7 cm diameter: the four IUWAs were placed at the corners of a 24 mm side square.

equally weighted. The average difference with its standard deviation is given in the lower left corner for each of the three diagrams. These average values indicate that simulation in fig.46 b) was the closest to the experimental hyperthermia. However the large standard deviation (close to 0.5°C) indicates that in all three cases significant individual differences between experiment and simulation occurred. Differences for T#1 to T#4 (describing temperature next to each applicator) are strongly influenced by the precision with which the thermistor location is known. Figs.49 a) and b) indicate that the simulations temperature elevations in the inner region (T#8, T#7 and T#6) were overestimated while for the same region the simulation of fig.46 c) gave better results. Experimental temperature elevations were higher than those from simulations at the outer boundary, T#5, in all three cases.

All simulations presented here used the five parameters discussed in the previous chapter: boundary temperatures τ_i and τ_o , the conduction coefficient k , the specific heat c and the source term $g(r)$. The extent of the hyperthermic field and its temperature distribution depended principally on the two boundary temperatures. Also, the value of the conduction coefficient has a strong effect. The distance separating the IUWAs, their power, g_o , and the medium effective thermal conductivity, k , influenced the temperature distribution. A hot spot or a highly uniform temperature in the central area were observed, depending on the values involved. Compared to the Aquasonic gel, the human brain tissue *in vitro* has a much lower k but its value increases in presence of the blood flow. Lower thermal conductivity and a lower τ_o occurs simultaneously and the applicability of the present results will depend on how effects of all these parameters will balance each other.

7. CONCLUSIONS AND FUTURE DIRECTIONS

The overall goal of this thesis was to evaluate critically the usefulness of the array of four interstitial ultrasonic waveguide applicators in delivering hyperthermia to brain tissue. The targeted temperature elevation of 6°C was intended to be produced uniformly over a large volume in as short time as possible.

Theoretical discussion of IUWA efficiency was related to the presence of surface waves. Longitudinal waves produced by IUWA piezoelectric were considered to be converted into two surface modes which propagate in the IUWA's waveguide. The unclad part of IUWA in acoustic contact with the medium radiated energy which was absorbed by the medium as heat. Heating effects depended in the first place on the waveguide radius. Small radius of the IUWA used in this study resulted in divergence effects much stronger than the effects of attenuation.

Effect of the cladding attached to the waveguide resulted in a minimal decrease of the acoustic output. Attenuation of the acoustic field along the IUWA's antenna was negligible. Each IUWA operated at its characteristic frequency could provide in many cases energy output in excess of the amount required to produce the targeted temperature elevation. Tuning of the IUWAs with inductors altered their OF, but a reduced output of the applicator was observed.

Hyperthermic temperature elevations were produced with one, two, three and four IUWAs in Aquasonic gel phantom tissue of substantial volumes from clinical standpoint. These temperature elevations were achieved in the gel phantom even though its thermal

conductivity coefficient was several times higher than that for brain tissue *in vitro*, and possibly comparable with that for brain tissue *in vivo*.

Hyperthermia simulations showed substantial enhancement in temperature elevation in the case of active heating (presence of sources) compared to passive heating (hot needles). Simulations indicated that for a medium with low k (as brain tissue *in vitro*) hyperthermic ranges and temperature elevation in the central region became quite large. For all simulations, the central region had markedly higher temperature elevation than the outer region, showing an important advantage of using the array. Although these heating effects were produced by superposition of weak sources, the power on the needles was sufficient to make the temperature elevation considerable.

Many of the issues in this study were addressed for the first time. Theoretical hypothesis, experimental and technical aspects, and simulations will need to be further developed.

The immediate improvement of IUWA manufacturing has to be addressed. This can increase applicators output, and bring their OFs values closer to each other. For increasing applicators output, both the acoustic transformer and the waveguide should be re-designed. Waveguides of larger diameters (up to 2 mm) would increase the intensity divergence and, hence, the absorbed power. Also an increase of the frequency at which piezoelectric is driven would increase the absorption coefficient with insignificant effects of an increase in attenuation. For these new conditions additional types of surface modes could be radiated into the medium. A major experimental challenge would be to improve

the shape of the acoustic transformer lateral surface to get a better efficiency of mode conversion. The RTV gluing procedure should be improved and the hard soldering of transformer to waveguide, if possible, avoided. The IUWAs holder should be re-designed to take into account its function as a cooling-down system. Depending on the thermal properties of the brain tissue *in vivo* and/or the geometry of the target region, other configurations of IUWAs in the array should be tried.

Hyperthermia produced with IUWAs array should be checked by measurements in brain tissue *in vitro* and *in vivo*. The blood perfusion term included in the effective thermal conduction coefficient would increase the thermal conduction of the brain tissue *in vivo*. The concurrent effects of this increase in effective thermal conduction coefficient and decreased temperature elevation at the outer boundary would show validity of the present results.

APPENDIX 1: TEST PROBLEM FOR FEA

Let's consider a homogeneous hollow cylinder of radius r_1 (inner) and r_2 (outer). Its length L is assumed sufficiently long such that the end effects are negligible. Temperature τ at any point in the medium $r_1 < r < r_2$ is supposed to be time independent for the steady state. No sources are present within the medium at any r , but boundaries are kept at constant temperatures $\tau(r_1) = \tau_i$, $\tau(r_2) = \tau_o$. Under these circumstances, heat conduction equation describing temperature at a point r in the medium becomes a 1-D problem which can be written as a second degree ordinary differential equation [44]:

$$\frac{d^2\tau}{dr^2} + \frac{1}{r} \cdot \frac{d\tau}{dr} = 0 \therefore \frac{d}{dr} \left(r \frac{d\tau}{dr} \right) = 0 \quad (\text{A1.1})$$

This equation can be solved directly by double integration. The two integration constants can be found from boundary conditions. Following these simple procedures, the final solution describing the temperature in the medium $\tau(r)$ is:

$$\tau(r) = \tau_i - \frac{\tau_i - \tau_o}{\ln \frac{r_2}{r_1}} \cdot \ln \frac{r}{r_1} \quad (\text{A1.2})$$

This analytic solution has been plotted for $\tau_i = 10^\circ\text{C}$ at $r_1 = 0.055$ cm (the used antenna radius) and $\tau_o = 0^\circ\text{C}$ at $r_2 = 1.32$ cm (the radius of vial, V#1). For the same conditions, simulated temperature field is presented in fig.38. For this simulation a conduction coefficient $k=0.0025$ W/cm°C and a specific heat $c=4.2$ J/g°C were assumed, although the

temperature distribution depends only on the inner and outer boundary temperatures. The two results are compared in fig.A1. Temperatures differed slightly only at the second decimal place, and this effect is believed to be caused by the relatively rough mesh used in simulation (equal spaced layers at step of 0.055 cm). Such difference is much smaller than experimental errors on temperature.

Figure A1: Analytic vs. FEM comparison

APPENDIX 2: ELASTIC CONSTANTS FOR SOME SOLIDS

Elastic constant values may differ from reference to reference. All the values presented here were taken from [9], pp.206-231. Values within brackets were calculated using formulae (9) or (10).

Table A2: Elastic constants for some solids

Elastic constant	Steel	Stainless steel 4130	Stainless steel 304L	Aluminium	Brass 70-30	Brass 70-30
v_l [m/s]	6100	5830	5640	~6250	4700	4370
v_t [m/s]	(3370)	(3130)	3070	~3100	2110	2100
σ	0.28	0.298	0.29	0.33	0.331	0.35
v_r [m/s]	(3120)	(2900)	(2840)	(~2890)	(1970)	(1960)
ρ [kg/m ³]	7700	-	7900	~2800	8600	8500

APPENDIX 3: ACOUSTIC IMPEDANCE FOR SOME MATERIALS

For plane waves, the acoustic impedance Z is related to the average power density in the direction of propagation $\langle \Pi \rangle$ [7]:

$$\langle \Pi \rangle = \frac{Z v_p^2}{2}$$

where v_p is the absolute value of particle velocity defined by (2). Eqs. (3), (6) or (8) give the acoustic impedance for different type of waves. The Table A3 gives the density, the phase velocity for longitudinal waves v_p , and the acoustic resistance for some reference materials and related to the piezoelectric-RTV-acoustic transformer interfaces. Data were taken from [7] pp.7-8 and for APC were calculated based on Table 1:

Table A3 : Acoustic impedance for some materials

Material	Density [kg/m ³]	v_p [m/s]	Z (x10 ⁶ kg/m ² s)
air at 20°C	1.21	340	0.000411
water at 20°C	1000	1480	1.5
silicone rubber (GE RTV 615)	1010	1030	1.04
stainless steel	8090	5610	45.4
brass	8100	4430	35.9
PZT- 5A	7750	4350	33.7
PZT- 5H	7500	4560	34.2
APC- 850	7500	4060	30.5

APPENDIX 4: REFLECTION AT THE COUPLING LAYER INTERFACES

Eq.(13) applies to fig.9 and describes the acoustic impedance Z encountered by the longitudinal wave emitted by the piezoelectric of impedance Z_0 , propagating through the RTV layer of impedance Z_2 and through the stainless steel transformer of impedance Z_3 . The RTV layer thickness, l_2 , is equal to half-wavelength in RTV at 1 MHz: $\lambda/2 = v_l/2f = 0.515$ mm (from Appendix 3). For this value, the condition $\tan(k_2 l_2) = 0$ holds when $k_2 = 6.1$ mm⁻¹, and eq.(13) reduces to $Z = Z_3$.

The reflection coefficient (rc) in eq.(14) will be significant if there is a mismatch between the acoustic impedance of the piezoelectric, Z_0 , and the acoustic impedance of the acoustic transformer, Z_3 . For $Z_3 \approx 45 \times 10^6$ kg/m²s and $Z_0 \approx 30 \times 10^6$ kg/m²s from Appendix 3, the half-wavelength coupling thickness yields a minimum back-reflection coefficient of $\approx 12\%$.

The worst matching scenario is when l_2 and k_2 give $\tan(k_2 l_2) = \infty$. In that case the total impedance given by (13) becomes complex and the back-reflection coefficient will be close to 100%. With the same value of $k_2 = 6.1$ mm⁻¹ this would happen at $l_2 = 0.772$ mm. The coupling layer thickness l_2 should be controlled very carefully.

APPENDIX 5: US AND THERMAL COEFFICIENTS FOR SOME TISSUES

US coefficients shown here are power absorption coefficient, a , and power attenuation coefficient, μ . Their units are [Np/cm] or [cm⁻¹] and for conversion into [dB/cm] one can use 1 dB = 8.686 Np. Absorption coefficient describes the conversion of sound energy into heat. Power attenuation includes beside absorption all types of energy loss as scattering, etc. and therefore $\mu \geq a$. These coefficients increase with the US frequency (which should be expressed in MHz). Values in columns three and four are given at 1 MHz and they depend on the experimental technique used for determination.

Table A5: US and thermal coefficients for brain, blood and water

Substance	Conditions	$a/2$	$\mu/2$	ρ	c_m	k	$\chi(10^{-5})$	Ref:
brain	37°C	$0.024 f^{1.18}$	$0.07 f^{1.14}$	1.03				[34]
brain	excised	same		1.05	3.9	0.0052	1.3	[11]
cat brain							0.5-1.3	[35]
brain	fresh		0.06	1.03				[33]
white matter		$0.064 f^{1.27}$						[23]
grey matter		$0.012 f^{1.21}$						[23]
mixture			$0.04 f^{1.17}$					[23]
blood	whole			1.05	4.0	0.0055	1.4	[11]
water	37°C	$0.00025f^2$				(0.0063)		[34]

Thermal coefficients are the density, ρ , in $[\text{g}/\text{cm}^3]$; the mass specific heat, c_m , in $[\text{J}/\text{g}^\circ\text{C}]$; the thermal conductivity, k , in $[\text{W}/\text{cm}^\circ\text{C}]$; and the thermal diffusivity, χ , in $[\text{cm}^2/\text{s}]$. From c_m one can find the volumic specific heat, $c_v = c_m \rho$, in $[\text{J}/\text{cm}^3^\circ\text{C}]$. Coefficients k and χ are related by: $\chi = k/(\rho c_m) = k/c_v$. These coefficients change slightly with temperature.

REFERENCES:

- [1] : B.J.Jarosz: "Temperature distribution in interstitial ultrasonic hyperthermia", Proc.I.E.E.E.Conf.Eng. Med.Biol., **13**, 178, 1991
- [2] : B.J.Jarosz: "Rate of heating in tissue in vitro by interstitial ultrasound", Proc.Ann.Int.I.E.E.E.Conf. Eng.Med.Biol.Soc., **12**, 274, 1990
- [3] : B.J.Jarosz: "Ultrasonic interstitial heating in phantoms", Proc.Ann.Int.Conf.I.E.E.E.Eng.Med.Biol.Soc., **11**, 1451-2, 1989
- [4] : B.J.Jarosz, R.L.Clarke: "Acoustic radiation from thin rods to water", Can.J.Phys, **64**, 671-6, 1986
- [5] : I.A.Viktorov: "Rayleigh and Lamb waves", Plenum Press, New York, 1967
- [6] : B.A.Auld: "Acoustic fields and waves in solids", Krieger P., Malabar, vol.II, 1990
- [7] : V.M.Ristic: "Principles of acoustic devices", Wiley, Toronto, 1983
- [8] : M.C.Junger, D.Feit: "Sound, structures and their interaction", MIT, Cambridge Mass, 1986
- [9] : D.Ensminger: "Ultrasonics", M.Dekker, New York, 1988
- [10] : G.M.Hahn: "Hyperthermia for the engineer: a short biological primer", I.E.E.E. Trans. Biomed. Eng., **BME-31**, **1**, 3-8, 1984
- [11] : NCRP Report #113: "Exposure criteria for medical diagnostic ultrasound:I.Criteria based on thermal mechanisms", 1992
- [12] : D.A.Christensen, C.H.Dumey: "Hyperthermia production for cancer therapy: a review of fundamentals and methods", J.Microwave Power, **16**, 89-105, 1981
- [13] : J.B.Keller: "Elastic waveguides", in: "*Modern problems in elastic wave propagation*", ed. J.Miklowitz and J.D.Achenbach, Wiley, New York, 1978, 401-415
- [14] : N.G.Brower, D.E.Himberger, W.G.Mayer: "Restrictions on the existence of leaky Rayleigh waves", I.E.E.E. Trans. Sonics. Ultrasonics, **SU-26**, 306-308, 1979

- [15] : K.Drantsfeld, E.Salzmam: "High-frequency elastic surface waves", in: *"Physical Acoustics principles and methods"*, vol.7, ed. W.P.Mason and R.N.Thurson, Academic Press, San Diego, 1970, 220-263
- [16] : M.C.Junger: "The physical interpretation of the expression for an outgoing wave in cylindrical coordinates", *J.Acoust.Soc.Am.*, **25**, 40-47, 1953
- [17] : M.C.Junger: "Dynamic behaviour of reinforced cylindrical shells in a vacuum and in a fluid", *J.Appl.Mech.*, **21**, 35-41, 1954
- [18] : S.Datta: "Surface acoustic waves devices", Prentice Hall, Englewood Cliffs N.J, 1986
- [19] : A.A.Oliner: "Microwave network methods for guided elastic waves", *I.E.E.E. Trans.M.T.T.*, **MTT-17**, 812-826, 1969
- [20] : L.D.Landau, E.M.Lifshits: "Fluid mechanics", Pergamon Press, London, 1959
- [21] : V.H.Kenner, W.Goldsmith: "Elastic waves in truncated cones", *Exper.Mech.*, **8**, 442-449, 1968
- [22] : T.R.Meeker, A.H.Meitzler: "Guided wave propagation", in: *"Physical acoustics principles and methods"*, vol.11, ed W.P.Mason, Academic Press, San Diego, 1964, 130-165
- [23] : M.E.Lyons, K.T.Parker: "Absorbtion and attenuation in soft tissues", *I.E.E.E.Trans.Ultrason.Fer.Freq. Control*, **UFFC-35**, 516-517, 1988
- [24] : G.R.Harris: "Hydrophone measurements in diagnostic ultrasound fields", *I.E.E.E.Trans.Ultrason. Fer.Freq.Control*, **UFFC-35**, 87-101, 1988
- [25] : W.J.Fry, R.B.Fry: "Determination of absolute sound levels and acoustic absorbtion coefficients by thermocouple probes- Theory and Experiment", *J.Acoust.Soc.Am.*, **26**, 294-317, 1954
- [26] : C.J.Diederich, K.Hynynen: "The development of intracavitary ultrasonic applicators for hyperthermia: a design and experimental study", *Med.Phys.*, **17**, 626-633, 1990
- [27] : K.Hynynen: "The feasibility of interstitial ultrasound hyperthermia", *Med.Phys.*, **19**, 979-987, 1992
- [28] : F.W.Wiegel: "Physical principles in chemoreception", Springer-Verlag, Berlin, 1991
- [29] : H.Kolsky: "Sstress waves in solids", Dover, New York, 1963
- [30] : B.J.Jarosz: "Ultrasound interstitial hyperthermia", review in: *Therapeutic application of ultrasound (minisymposium)*, Proc.16th Ann.Intl.Conf.IEEE Eng.Med.Biol.Soc, 1994.

- [31] : G.P.Raaphorst, A.Bussey, D.P.Heller, C.E.Ng: "Comparison of thermoradiosensitization in two human melanoma cell lines and one fibroblast cell line by concurrent mild hyperthermia and low-dose-rate irradiation". *Radiation Research*, **137**, 338-345, 1994
- [32] : J.Crezee, J.Mooibroek, J.J.W.Legendijk, G.M.J.van Leeuwen: "The theoretical evaluation of the heat balance in perfused tissue". *Phys.Med.Biol.*, **39**, 813-832, 1994
- [33] : D.A.Cristensen: "Ultrasonic bioinstrumentation". Wiley, Toronto, 1988, p.61
- [34] : P.D.Edmons(ed.): "Ultrasonics", in: "*Methods of experimental physics*", vol.19, ed. L.Marton and C.Marton, Academic Press, Toronto, 1981, 12-14
- [35] : Y.S.Touloukian: "Thermal conductivity. metallic elements and alloy", IFI, New York, 1970
- [36] : L.E.Kinsler, A.R.Frey: "Fundamentals of acoustics", Wiley, New York, 1961, pp.217-245
- [37] : C.J.Diederich, K.H.Hynynen: "Ultrasound technology for interstitial hyperthermia", in: "*Medical radiology*", eds. L.W.Brady and H.P.Heilmann, Springer-Verlag, Berlin, 1993, 55-61
- [38] : J.W.Smith, W.E.Jackson, E.P.Clark, G.P.Raaphorst: "Oncogenic potential of hyperthermia in combination to radiation", *Int.J.Hyperthermia*, **10**, 429-432, 1994
- [39] : K.Hynynen, K.L.Davies: "Small cylindrical ultrasound sources for induction of hyperthermia via body cavities or interstitial implants", *Int.J.Hypth*, **9**, 263-274, 1993
- [40] : R.C.Miller, M.Richards, C.Baird, S.Martin: "Interaction of hyperthermia and chemotherapy agents: cell lethality and oncogenic potential", *Int.J.Hypth*, **10**, 89-99, 1994
- [41] : Z.P.Chen, R.B.Roemer, T.C.Cetas: "Three-dimensional simulations of ferromagnetic implant hyperthermia", *Med.Phys*, **19**, 989-997, 1992
- [42] : M.Kikuchi, Y.Amemiya, S.Egawa, Y.Onoyama, H.Kato, H.Kanai, Y.Saito, I.Tsukiyama, M.Hiraoka, S.Mizushina, T.Yamashita: "Guide to the use of hyperthermia equipment. 1. Capacitively- coupled heating", *Int.J.Hypth*, **9**, 187-203, 1993
- [43] : same authors plus Y.Nikawa, J.Matsuda, M.Miyakawa: "Guide to the use of hyperthermia equipment. 2. Microwave heating", *Int.J.Hypth*, **9**, 341-360, 1993
- [44] : S.Kakac: "Heat conduction", Hemisphere, Washington D.C, 1985, pp.53-54

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