

Simulation of the Thermal and Mechanical Effects of a Planar Rectangular High Intensity Ultrasound Transducer to Be Used for Destroying Atherosclerotic Plaque

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Received June 2013

ABSTRACT

The aim of this study is to perform a simulation study of the thermal and mechanical effects of a flat rectangular ($3 \times 10 \text{ mm}^2$), MRI compatible transducer operating at 5 MHz for the purpose of destroying atherosclerotic plaque. The simulation study focuses on measuring the plaque destruction (due to the thermal of mechanical mode of ultrasound) as a function of power, time, frequency, duty factor and pulse duration. The main goal is to keep the artery temperature at a safe level. The simulation study shows that with the thermal mode the temperature in the artery cannot be kept at a safe level.

Keywords: Ultrasound; Atherosclerotic; Plaque; MRI

1. Introduction

Atherosclerosis also known as arteriosclerotic vascular disease (ASVD) is a condition in which fatty material collects along the walls of arteries. This fatty material thickens, hardens (forms calcium deposits), and may eventually block the arteries [1]. Calcium is a critical component of atherosclerotic plaque. The absence of calcification is strong evidence against the presence of active disease even with significant luminal stenosis. Calcification is reversible and may contribute to the formation of an atheroma by adding the byproducts of resorption to the necrotic core. The sequence of events in plaque development following injury is inflammation, followed by calcification of the damaged tissue, ending ultimately in the formation of a necrotic core [2-4].

Lifestyle changes, such as following a healthy diet and exercising, are often the best treatment for atherosclerosis. But sometimes, medication or surgical procedures may be recommended as well [5]. Over the years, researchers have been involved in Clinical research to develop medication treatments and approaches in order to reduce the risk of heart attack and other medical problems caused by atherosclerosis (for example Angiotensin II receptor blockers (ARBs) [5], Angiotensin-converting enzyme (ACE)[6], Cholesterol Medications[7], Diuretics[8]). In advanced cases, atherosclerosis treatment may require special surgical procedures such as Balloon Angioplasty [9-12], Balloon Angioplasty and Stenting [13-15], Cutting Balloon [16-21], Atherectomy [22,23], Surgical Bypass [24,25] and Endarterectomy [26,27] to open an artery and improve blood flow.

Another treatment option could be the application of mechanical waves such as ultrasound. With ultrasound either the thermal or mechanical properties can be utilized. Our group uses MRI to monitor ultrasonic protocols and therefore, the ultrasonic transducer has to be MRI compatible. In this paper a simulation study of the thermal and mechanical effects of flat rectangular (3×10 mm²), MRI compatible ultrasonic transducer operating at 5 MHz for destroying atherosclerotic plaque is included. The simulation study focuses on measuring the plaque destruction (thermal of mechanical) as a function of power, time, frequency, duty factor and pulse duration. The main goal is to keep the artery temperature at a safe level. This paper includes the design of the MRI compatible transducer.

2. Materials and Methods

2.1. Simulation Model

The power field was estimated using the KZK model [28]. The temperature vs. time history was obtained by

solving the bio-heat equation proposed by Pennes (1948) numerically [29]. The explicit form of this equation is given by:

$$p_t c_t \frac{\partial T}{\partial t} = k \nabla^2 T + w_{bcb} (T - T_a) + Q_p \tag{1}$$

where ρ_t is the density of the tissue, c_t is the specific heat of the tissue, T is the temperature of the tissue, t is the time, w_b is the blood perfusion rate, c_b is the specific heat of the blood, T_a is the arterial blood temperature, k is the thermal conductivity of the tissue, and Q_p is the ultrasonic power deposition rate.

2.2. Estimation of Thermal Dose

The effect of hyperthermia depends on the temperature and the duration of the heating. If a constant temperature could be maintained, then the duration of heating would be a reasonable way of expressing thermal dose, with units of time. In reality, however, a constant temperature is not maintained, so it is necessary to find a method of relating a treatment to an equivalent time at a specified reference temperature. A mathematical relation between time and temperature was described by Dewey [30] and given by:

$$t_{2} = t_{1} R^{(T_{2} - T_{1})}, \tag{2}$$

where T_1 , T_2 are temperatures at times t1 and t2 respectively, and R is a constant.

The calculation of the thermal dose for changing temperature exposure was done by using the technique suggested by Sapareto and Dewey [31]. The technique uses numerical integration to calculate the time that would give an equivalent thermal dose at a reference temperature under different temperature profiles. The reference temperature of 43°C has been chosen since this is the standard temperature used as a reference [21]. For any temperature profile the dose can be found by

$$t_{43} = \sum_{0}^{tfinal} R^{(43-T_t)} \Delta t, \qquad (3)$$

where t_{43} is the equivalent time at 43°C, T_t is the average temperature during Δt . The default value of R equal to 0.25 was chosen for temperatures smaller than 43°C and a value equal to 0.5 for temperatures higher than 43°C [31]. The temperature after the power turn OFF was also considered since during the decay part thermal dose is contributed.

2.3. Estimation of Lesion Size

The prediction of lesion size requires the knowledge of the thermal dose threshold that causes 90% - 100% necrosis. Previous studies [32,33] show that the threshold thermal dosage reference at 43°C for soft tissue is be-

tween 50 min and 240 min. Therefore, the extreme threshold of dose necrosis of 240 min at 43° C was considered.

3. Results

Figure 1 shows the graph of thermal lesion vs. power for a 20 s sonication at the frequency of 5, 6, 7 MHz. Therefore with 5 MHz and 3 W a plaque of 2 mm is destroyed. With 7 MHz a power of 6 W must be used in order to destroy 2 mm. Figure 2 shows the thermal lesion vs. time for a power of 7 W at the frequency of 5, 6, 7 MHz. Therefore with 5 MHz and 20 s a 4 mm plaque is destroyed. With 7 MHz and 20 s a plaque of 2 mm is destroyed. The temperature in the artery for both Figure 1 and Figure 2 exceeded the safe level. Figure 3 shows the graph of plaque removal vs. power for PRF = 1 Hz, DF =10% and frequency 5, 6, 7 MHz (total time = 30 mins). Therefore with 5 MHz and 60 W a plaque of 2 mm is removed. With 7 MHz and 60 W a 1 mm plaque is removed. The temperature in the artery for the results of Figure 3 never exceeded the safe level.

4. Conclusions

The aim of this paper was to conduct a simulation study

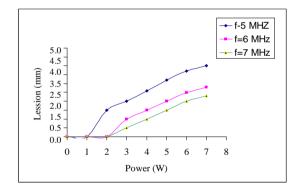


Figure 1. Thermal lesion vs. power for a 20 s sonication at the frequency of 5, 6, 7 MHz.

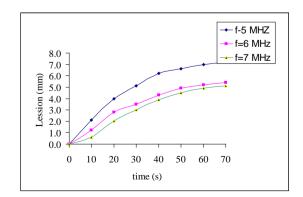


Figure 2. Thermal lesion vs. time for a power of 7 W at the frequency of 5, 6, 7 MHz.

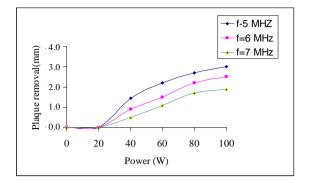


Figure 3. Plaque removal vs. power for PRF = 1 Hz, DF = 10% and frequency 5, 6, 7 MHz (total time = 30 min).

of the thermal and mechanical effects of a flat rectangular $(3 \times 10 \text{ mm}^2)$ MRI compatible transducer operating at 5 MHz for destroying atherosclerotic plaque. The main goal was to keep the artery temperature at a safe level. The simulation study shows that with the thermal mode the temperature in the artery cannot be kept at a safe level. Using mechanical mode ultrasound yields no severe temperature elevation in the arteries. This paper provides useful information regarding the size of the plaque removal as power, time, frequency, duty factor and pulse duration.

5. Acknowledgements

This work was supported by the Research Promotion Foundation of Cyprus and the European regional development structural funds (project number EIIIXEIPH Σ EI Σ / IIPOÏON/0311/01).

REFERENCES

- [1] L. Wagenknecht, B. Wasserman, L. Chambless, J. Coresh, A. Folsom, T. Mosley, C. Ballantyne, R. Sharrett and E. Boerwinkle, "Correlates of Carotid Plaque Presence and Composition as Measured by Magnetic Resonance Imaging: The Atherosclerosis Risk in Communities (Aric) Study Wagenknecht, Risk Factors & Mri Measured Carotid Plaque," *Circulation: Cardiovascular Imaging*, Vol. 2, No. 4, 2009, pp. 314-322. <u>http://dx.doi.org/10.1161/CIRCIMAGING.108.823922</u>
- [2] L. Wexler, B. Brundage, J. Crouse, R. Detrano, V. Fuster, J. Maddahi, J. Rumberger, W. Stanford, R. White and K. Taubert, "Coronary Artery Calcification: Pathophysiology, Epidemiology, Imaging Methods, and Clinical Implications," *Circulation*, Vol. 94, 1996, pp. 1175-1192. http://dx.doi.org/10.1161/01.CIR.94.5.1175
- [3] T. J. Romer, J. F. Brennan, M. Fitzmaurice, M. L. Feldstein, G. Deinum, J. L. Myles, J. R. Myles, J. R. Kramer, R. S. Lees and M. S. Feld, "A Rotational Ablation Tool for Calcified Atherosclerotic Plaque Removal Biomedical Microdevices," *Circulation*, Vol. 97, 1998, p. 8.
- [4] M. Naghavi, P. Libby, E. Falk, S. W. Casscells, S. Li-

tovsky and J. Rumberger, "From Vulnerable Plaque to Vulnerable Patient: A Call for New Definitions and Risk Assessment Strategies: Part I," *Circulation*, Vol. 108, 2003, pp. 1664-1672.

http://dx.doi.org/10.1161/01.CIR.0000087480.94275.97

- [5] Y. Nishida, Y. Takahashi, T. Nakayama and S. Asai, "Comparative Effect of Angiotensin II Type I Receptor Blockers and Calcium Channel Blockers on Laboratory Parameters in Hypertensive Patients with Type 2 Diabetes," *Cardiovascular Diabetology*, Vol. 11, No. 3, 2012, p. 53. <u>http://dx.doi.org/10.1186/1475-2840-11-53</u>
- [6] H. Q. Li, Y. Li, C. Wang, T. Sun, Z. M. Sun, J. Zhou, L. Ba and Z. Z. Huang, "Study on the Association of Oral Contraceptives, Angiotensin-Converting Enzyme Gene Polymorphisms and Risk of Stroke in Women," *Zhong-hua Liu Xing Bing Xue Za Zhi*, Vol. 33, No. 1, 2012, pp. 23-27.
- H. R. Superko, K. M. Momary and Y. Li, "Statins Personalized," *Medical Clinics of North America*, Vol. 96, No. 1, 2012, pp. 123-139. http://dx.doi.org/10.1016/j.mcna.2011.11.004
- [8] Y. Matsui, M. F. O'Rourke, S. Hoshide, J. Ishikawa, K. Shimada and K. Kario, "Combined Effect of Angiotensin II Receptor Blocker and Either a Calcium Channel Blocker or Diuretic on Day-by-Day Variability of Home Blood Pressure: The Japan Combined Treatment With Olmesartan and a Calcium-Channel Blocker Versus Olmesartan and Diuretics Randomized Efficacy Study," *Hypertension*, Vol. 59, No. 6, 2012, pp. 1132-1138. http://dx.doi.org/10.1161/HYPERTENSIONAHA.111.18 9217
- [9] B. Mc Cutcheon, D. Weatherford, G. Maxwell, et al., "A Preliminary Investigation of Balloon Angioplasty Versus Surgical Treatment of Thrombosed Dialysis Grafts," *The American Journal of Surgery*, Vol. 69, 2003, pp. 663-667.
- [10] J. Ziv. Haskal, S. Trerotola, B. Dolmatch, E. Schuman, S. Altman, S. Mietling, S. Berman, G. McLennan, C. Trimmer, J. Ross and T. Vesely, "M.D. Stent Graft versus Balloon Angioplasty for Failing Dialysis-Access Grafts N," *The New England Journal of Medicine*, Vol. 362, 2010, pp. 494-503.
- [11] S. Rafajlovski, V. Orozović, A. Ristić-Andelkov and G. Raden, "Percutaneous Transluminal Coronary Angioplasty in the Right Ventricle Myocardial Infarction Treatment," *Vojnosanit Pregl*, Vol. 62, No. 10, 2005, pp. 731-738. <u>http://dx.doi.org/10.2298/VSP0510731R</u>
- [12] M. D. Dake, G. M. Ansel, M. R. Jaff, T. Ohki, R. R. Saxon, H. B. Smouse, T. Zeller, G. S. Roubin, M. W. Burket, Y. Khatib, S. A. Snyder, A. O. Ragheb, J. K. White and L. S. Machan, "Paclitaxel-Eluting Stents Show Superiority to Balloon Angioplasty and Bare Metal Stents in Femoropopliteal Disease: Twelve-Month Zilver PTX Randomized Study Results," *Circulation: Cardiovascular Interventions*, 2011.
- [13] C. J. Boyle, A. B. Lennon and P. J. Prendergast, "In silico prediction of the mechanobiological response of arterial tissue: application to angioplasty and stenting," *Journal* of Biomechanical Engineering, Vol. 133, No. 8, 2011. http://dx.doi.org/10.1115/1.4004492

- 350
- [14] T. Abu-Tair, C. Martin and C. Kampmann, "Acute Aortic Dissection after Balloon Angioplasty of a Recoarctation and Treatment by Stenting and Distal Membrane Fenestration in a Child," *Heart*, Vol. 97, No. 20, 2011, pp. 1699-1700. http://dx.acute.com/10.1126/heartinl.2011.200700

http://dx.doi.org/10.1136/heartjnl-2011-300709

- [15] H. Takebayashi, S. Haruta, H. Kohno, *et al.*, "Immediate and 3-Month Follow-Up Outcome after Cutting balLoon Angioplasty for Bifurcation Lesions," *Journal of Interventional Cardiology*, Vol. 17, 2004, pp. 1-7. http://dx.doi.org/10.1111/j.1540-8183.2004.00246.x
- [16] L. J. Bergersen, S. B. Perry and J. E. Lock, "Effect of Cutting Balloon Angioplasty on Resistant Pulmonary Artery Stenosis," *American Journal of Cardiology*, Vol. 15, 2003, pp. 185-189. http://dx.doi.org/10.1016/S0002-9149(02)03107-7
- [17] J. F. Rhodes, G. K. Lane and C. I. Mesia, "Cutting Balloon Angioplasty for Children with Small-Vessel Pulmonary Artery Stenoses," *Circulation: Cardiovascular Interventions*, Vol. 55, 2002, pp. 73-77. http://dx.doi.org/10.1002/ccd.10031
- [18] G. M. Ansel, N. S. Sample, C. F. Botti III Jr, et al., "Cutting Balloon Angioplasty of the Popliteal and Infrapopliteal Vessels for Symptomatic Limb Ischemia," Circulation: Cardiovascular Interventions, Vol. 61, 2004, pp. 1-4. http://dx.doi.org/10.1002/ccd.10731
- [19] C. Engelke, C. Sandhu, R. A. Morgan, *et al.*, "Using 6-mm Cutting Balloon Angioplasty in Patients with Resistant Peripheral Artery Stenosis: Preliminary Results," *AJR*, Vol. 179, 2002, pp. 619-623. <u>http://dx.doi.org/10.2214/ajr.179.3.1790619</u>
- [20] K. Kasirajan and P. A. Schneider, "Early Outcome of "Cutting" Balloon Angioplasty For Infrainguinal Vein Graft Stenosis," *Journal of Vascular Surgery*, Vol. 39, 2004, pp. 702-708. http://dx.doi.org/10.1016/j.jvs.2003.10.046
- [21] R. D. Safian, C. L. Grines, M. A. May, A. Lichtenberg, N. Juran, T. L. Schreiber, G. Pavlides, T. B. Meany, V. Savas and W. W. O'Neill, "Clinical and Angiographic Results of Transluminal Extraction Coronary Atherectomy in Saphenous Vein Bypass Grafts," *Circulation*, Vol. 89, 1994, pp. 302-312. http://dx.doi.org/10.1161/01.CIR.89.1.302
- [22] F. Mangiacapra, G. R. Heyndrickx, E. Puymirat, A. J. Peace, W. Wijns, B. De Bruyne and E. Barbato, "Comparison of drug-Eluting Versus Bare-Metal Stents after Rotational Atherectomy for the Treatment of Calcified Coronary Lesions," *International Journal of Cardiology*, Vol. 153, No. 3, 2012, pp. 373-376. http://dx.doi.org/10.1016/j.ijcard.2011.11.048
- [23] S. K. Forouzannia, M. H. Abdollahi, S. J. Mirhosseini, H. Hosseini, S. H. Moshtaghion, A. Golzar, N. Naserzadeh, S. M. Ghoraishian and T. Emami Meybodi, "Clinical Outcome and Cost in Patients with Off-Pump vs. On-Pump Coronary Artery Bypass Surgery," *Acta Medica Iranica*, Vol. 49, No. 7, 2011, pp. 414-419.

- [24] E. J. Lee, K. H. Choi, J. S. Ryu, S. B. Jeon, S. W. Lee, S. W. Park, S. J. Park, J. W. Lee, S. J. Choo, C. H. Chung, S. H. Jung, D. W. Kang, J. S. Kim and S. U. Kwon, "Stroke Risk after Coronary Artery Bypass Graft Surgery and Extent of Cerebral Artery Atherosclerosis," *American College of Cardiology Foundation*, Vol. 57, No. 18, 2011, pp. 1811-1818. http://dx.doi.org/10.1016/j.jacc.2010.12.026
- [25] J. T. McGinn Jr, M. A. Shariff, T. M. Bhat, B. Azab, W. J. Molloy, E. Quattrocchi, M. Farid, A. M. Eichorn, Y. D. Dlugacz and R. A. Silverman, "Prevalence of Dysglycemia among Coronary Artery Bypass Surgery Patients with No Previous Diabetic History," *Journal of Cardiothoracic Surgery*, Vol. 6, 2011, p. 104. http://dx.doi.org/10.1186/1749-8090-6-104
- [26] A. Redzek, B. Mihajlović, P. Kovacević, N. C. Adić, K. Pavlović, L. Velicki, "Patency of internal thoracic artery and vein grafts according to revascularized coronary artery properties," Med Pregl., Vol. 64, No. 3-4, 2011, pp. 137-142. <u>http://dx.doi.org/10.2298/MPNS1104137R</u>
- [27] A. Siani, F. Accrocca, L. M. Siani, R. Gabrielli, R. Antonelli, G. A. Giordano and G. Marcucci, "Prosthetic Carotid Bypass Graft for In-Stent Restenosis Performed for Post-Endarterectomy Recurrent Stenosis: Technical Details," *Giornale di Chirurgia*, Vol. 33, No. 3, 2012, pp. 95-97.
- [28] R. J. McDonald, H. J. Cloft and D. F. Kallmes, "Intracranial Hemorrhage is Much More Common after Carotid Stenting than after Endarterectomy: Evidence from the National Inpatient Sample," *Stroke*, Vol. 42, No. 10, 2011, pp. 2782-7278.
 - http://dx.doi.org/10.1161/STROKEAHA.111.618769
- [29] J. E. Soneson and M. R. Myers, "Gaussian representation of High-Intensity Focused Ultrasound Beams," *Journal of the Acoustical Society of America*, Vol. 122, No. 5, 2007, pp. 2526-2531.
- [30] M. Pennes, "Analysis of Tissue and Arterial Blood Temperature in the Resting Human Forearm," *Journal of Applied Physics*, Vol. 1, 1948, pp. 93-122.
- [31] W. Dewey, L. Hopwood, S. Sapareto and L. Gerwecki, "Cellular Responses to Combinations of Hyperthermia and Radiation," *Radiology*, Vol. 123, 1977, pp. 463-474.
- [32] S. Sapareto and W. Dewey, "Thermal Dose Determination in Cancer Therapy," *International Journal of Radiation Oncology Biology Physics*, Vol. 10, 1984, pp. 787-800. <u>http://dx.doi.org/10.1016/0360-3016(84)90379-1</u>
- [33] W. Jansen and J. Haverman, "Histological Changes in the Skin and Subcutaneous Tissues of Mouse Legs after Treatment with Hyperthermia," *Pathology: Research and Practice*, Vol. 186, 1983, pp. 247-253. <u>http://dx.doi.org/10.1016/S0344-0338(11)80542-X</u>