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# Design Issues for Therapeutic Ultrasound Angioplasty Waveguides

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# DESIGN ISSUES FOR THERAPEUTIC ULTRASOUND ANGIOPLASTY WAVEGUIDES

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## ABSTRACT

Therapeutic ultrasound angioplasty is a new minimally invasive cardiovascular procedure for disrupting atherosclerotic lesions. Mechanical energy is transmitted in the form of ultrasound waves via long, flexible wire waveguides navigated to the lesion site through the vascular system. The underpinning principle of this technology is that plaque may be disrupted through a combination of direct contact ablation, pressure waves, cavitation and acoustic streaming, which all depend on the amplitude and frequency of displacements at the distal tip of the wire waveguide. This study identifies a number of key design issues for clinical devices of this type, and describes testing procedures to measure selected performance characteristics. A commercially available generator (100 W) and acoustic horn are used in combination with Nickel-Titanium (NiTi) wire waveguides. A laser sensor system was constructed to measure the frequency and amplitude output at the distal tip of the wire waveguide, and this was compared to amplitude estimations obtained using an optical microscope. Power was observed to affect both output amplitude and frequency. A finite element model has been previously developed to simulate the transmission of ultrasound waves in short wire waveguides. In this study, this methodology has been extended to the design of long, tapered wires for realistic clinical applications. Trials were conducted using these wire waveguides, demonstrating the ablation of model calcified materials accessed via long wire waveguides.

**KEYWORDS: ultrasound, angioplasty, frequency**

## 1. INTRODUCTION

Coronary heart disease involves the narrowing or blocking of the coronary arteries, resulting in a reduction of blood flow. To restore luminal blood flow, the blockage must be de-bulked, removed or, in severe cases, by-passed. Key transluminal procedures, such as balloon angioplasty or stenting, rely on being able to advance a guidewire through and beyond the lesion site. Recanalisation of coronary arteries with chronic total occlusions (CTOs) remains, however, one of the most challenging interventional procedures faced by cardiologists. Chronic total occlusion of the right coronary artery has been identified in approximately 20% of angioplasty patients, and angioplasty of the CTO has been attempted in between 10-15% of all cases [1]. However, standard techniques, using contemporary guidewires, are unsuccessful in approximately 20% of these cases [2, 3].

There are currently a number of different guidewires on the market, with various degrees of success in crossing CTOs [4]. The majority of these have a main shaft diameter of 0.35mm or less. Their tips vary from 0.2mm-0.35mm in diameter [4]. These guidewires are classified as soft, intermediate or stiff. Soft wires are normal used for advancement of the catheter and crossing occlusions with small lumens. Intermediate wires are used for recently occluded lesions or tortuous vessels and stiff wires are used for advancing through CTOs.

Several devices have been developed in an attempt to improve CTO success rate, including a 20 kHz ultrasound wire waveguide device which delivers high power low frequency intravascular ultrasonic energy to the sites of chronic total occlusions [5]. Such a device received regulatory approval in Europe in 2005, and by the FDA in the U.S. in 2007.

Development of this technology began in earnest during the 1980s, when two groups, headed by Siegel and by Rosenschein respectively, pursued the objective of producing a working prototype for initial clinical testing and use in trials. Both teams based their design efforts on the system developed by Sobbe *et al* [6], delivering the ultrasonic waves to the lesion via a wire waveguide. These prototypes set up stress and displacement waves along the wire, resulting in ultrasonic displacement amplitudes in the micron range at the distal-tip of the wire waveguide.

The underlying principle of this technology is that the vibrating distal tip of the ultrasound wire waveguide is used to transmit energy to the surrounding fluids and tissues. Four primary mechanisms of interaction have been identified in the literature [7]; (i) acoustic pressure fluctuations, (ii) cavitation, (iii) acoustic streaming of blood and (iv) ablation due to direct contact with the distal tip. Using the right combination of frequency and amplitude, the ultrasound vigorously disrupts inelastic tissue while healthy tissue in the same region remains undamaged [8]. It was conceived that this form of energy may be useful in disrupting cardiovascular lesions, especially rigid calcified and fibrous plaques, and would have advantages over standard procedures such as angioplasty or atherectomy.

Siegel *et al* presented experimental *in vitro* studies and initial clinical experience with a 19.5 kHz ultrasonic waveguide for occluded coronary arteries [9]. This prototype appears to have laid the foundation for the development towards commercialisation of the current clinical device. In this study, the amplitude of vibration of the 1.7 mm ball tip was between 15 and 30 microns (30 $\mu$m to 60 $\mu$m peak to peak). 11 post mortem arteries were successfully recanalised, with the assistance of a firm pressure applied to the ultrasonically activated wire (stated to be between 100g and 200g based on a dynamometer measurement). Histological analysis of the recanalised vessels showed no evidence of thermal damage. Increased distensibility of the *in vitro* calcified arteries following two minutes exposure to the ultrasonic energy was also observed [9]. In the same publication by Siegel *et al*, 19 clinical cases were also reported, three with unstable angina and sixteen with exercise induced ischemia [9]. In 17 of these cases, the stenosis was reduced.

In later years, a number of clinical trials have been conducted with the recently launched clinical device. In one trial, 55 CTO's in 53 patients were treated using the system. The device showed a success rate of 76% with no major cardiac events or coronary perforation. In a second study with 30 lesions in 28 patients success was achieved in 63% of procedures [5]. One guidewire perforation was reported, with no serious adverse effects, and one peri-procedural myocardial infarction.

Despite increasing clinical acceptance of this technology, there has been little discussion of device design and verification issues. The primary mechanisms of ablation identified in the literature all depend on the amplitude and frequency of the vibrating waveguide distal tip. There is therefore an obvious need for systems to verify these output characteristics, and investigate their dependence on operating conditions and geometric factors. The first objective of this study, therefore, is to design a system to fully characterise the output of a prototype waveguide apparatus. Optical measurements of the distal tip peak-to-peak amplitudes have previously been made by means of an optical microscope, digital camera and computer with image analysis [11]. There are a number of limitations to this method. Firstly, only the maximum and minimum peak positions of the tip over the measurement interval are detected, and it is not determined whether these are achieved in every cycle. Secondly the optical method has an accuracy of approximately ±3-4 μm [11]. In applications with peak-to-peak displacements in the range of 20-40 μm, this represents a potentially significant error. Finally, no information about frequency changes or other harmonics during apparatus operation can be determined. This is an extremely important aspect, as the behaviour of the waveguide, and its interactions with fluids for example, is frequency dependent. In this study, a fibre-optic laser sensor system is used to measure output amplitudes and frequencies.

The design of long, low profile flexible wire waveguides to successfully transmit ultrasound waves along tortuous pathways also presents new mechanical design issues. Ultrasound waves travelling in a metal waveguide will be attenuated in accordance with the material's damping properties. A superelastic alloy (NiTi) has been selected to minimise this effect, but an earlier study has shown that damping can be observed even in relatively short NiTi waveguides [11]. While the distal wire section must be of sufficiently low profile to access the coronary arteries (0.20 to 0.35 mm are typical values [4]), a larger diameter proximal section is needed to provide a reliable connection to the acoustic horn [12]. Waveguide lengths of the order of 1600 mm may be required to access coronary arteries. The design concept explored in this study involves the use of taper sections to reduce the wire diameter at discrete intervals along its length. These tapers will have the effect of amplifying the ultrasound wave, ameliorating to some extent the attenuation effect. The lower mass of the distal sections should also help minimise damping. The second objective of this study, therefore, is to develop a design methodology for ultrasound wire waveguides with discrete taper sections, and with length and distal geometry characteristics suitable for minimally invasive coronary procedures.

## 2. MATERIALS AND METHODS

This study is conducted using a commercially available generator and acoustic horn, in combination with a Nickel-Titanium (NiTi) wire waveguides. The initial development of this experimental system for short wire waveguides (of the order of 300 mm) is described in detail elsewhere [11,12]. The acoustic horn transmits ultrasonic waves down a wire waveguide resulting in displacements of the distal tip at ultrasonic frequencies.

### 2.1 Laser Sensor System

A laser sensor system was developed to overcome some of the shortfalls with the optical measurement method. The system used in the measurement of the wire waveguide displacements is shown in Figure 1. It consists of a Laser sensor, an Oscilloscope and a PC with data acquisition card and software. The sensor chosen is a D6-HiTi Type D reflectance dependent fibre optic displacement sensor from Philtec Inc. This is a reflectance dependent non-contact sensor with a target surface size of 0.16mm$^2$. The sensor is capable of sampling up to 200kHz., and has a 0-1mm measurement range. The laser sensor has been calibrated with respect to polished Ni-Ti, and has a sensitivity in the linear range is 22.67μV/μm.

The movement of the sensor tip is controlled by a micrometer, which has a minimum displacement of 0.01mm. The data is obtained using the LabVIEW program. The data is then processed with a Fast Fourier Transform (FFT) algorithm to determine frequency changes.

### 2.2 Finite Element Analysis

The finite element analysis software ANSYS is used to model ultrasound wave transmission in waveguides. A 2D axisymmetric model using 4 node quadrilateral structural elements (Plane42) is used.

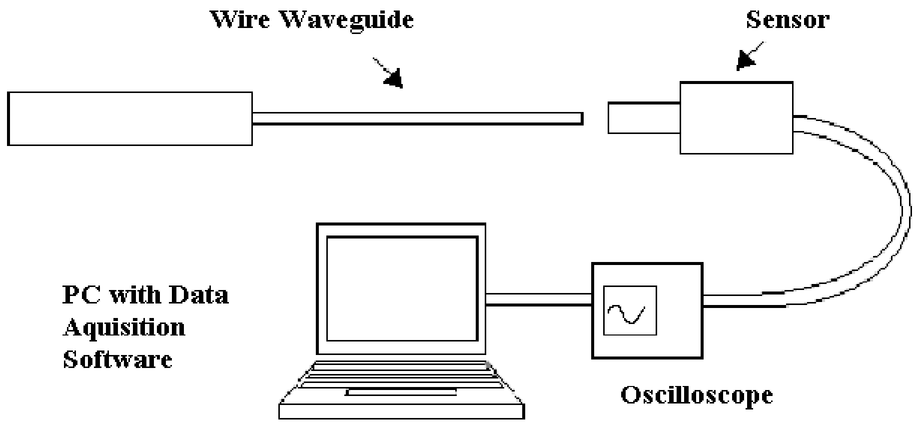


**Figure 1:** Wire waveguide displacement measurement set up with laser sensor, hardware low band pass filter and PC with data acquisition software

### 2.3 Tapered NiTi Wires

NiTi wires were obtained from Fort Wayne Metals (Fort Wayne, IN 46809, USA).

## 3. METHODOLOGY

### 3.1 Laser Sensor Measurements

The sensor was calibrated by the manufacturer with respect to a polished mirror surface, which would return a maximum of 5V for a 0.18mm gap between sensor tip and measuring surface. However, the reflectance properties of polished Nickel Titanium (NiTi) are much less than that of a mirrored surface, returning a maximum of 2.5V. To recalibrate the sensor, the output was connected to an ohmmeter and the sensor tip was placed directly in front of the distal tip of the polished Ni-Ti wire waveguide with no gap between the two tips. The sensor tip was then retracted in increments of 0.01mm measured by micrometer over a 1 mm range to obtain a displacement-voltage curve that could be used to determine distal tip displacements.

The recalibrated sensor was then used to determine change in frequencies and amplitudes of the NiTi wire waveguide 278mm in length and 1mm diameter. Measurements from the laser sensor were made by recording 0.1 seconds of data. The first 0.05miliseconds removed from the overall data, and the root mean square of the remaining data is determined.

### 3.2 Wire Waveguide Design Methodology

A finite element model for wave transmission in short, uniform cross section, wire waveguides with damping has previously been developed [11-13]. With reference to Figure 2, the challenge in this study is to determine lengths for sections 1, 2, 3, 4 and 5 which provide ultrasound wave transmission over lengths of up to 1600 mm. The diameters of sections 1, 3 and 5 were selected on practical grounds, relating to the geometric requirements of the application.

A 1.0mm proximal wire diameter was selected in order to provide a reliable connection to the acoustic horn. For 1.0 mm diameter NiTi wire waveguides, experiments have shown that ultrasound is not effectively transmitted over lengths greater then 330mm (corresponding to a wire weight of 1.67grams). To minimise damping, it is therefore desirable that the 1.0 mm section be as short as possible. A diameter of 0.35 mm is selected for Section 3, reflecting the requirement for a balance between the flexibility required to accommodate to the tortuous geometry of the vasculature and the rigidity needed for pushability. A diameter of 0.20 mm is chosen for Section 5, to facilitate maximum access to stenosed coronary arteries.

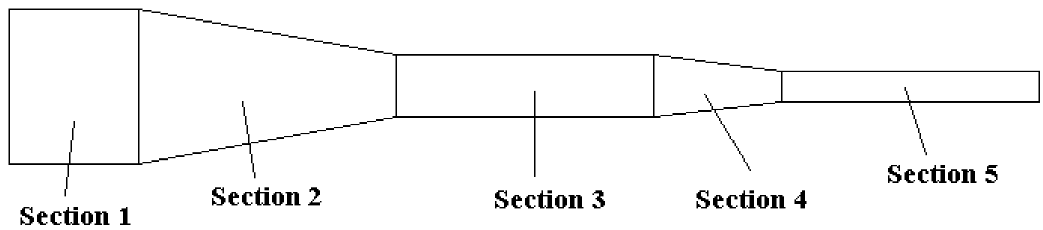


**Figure 2: Tapered wire configuration**

The uniform cross-section waveguide sections will be designed to be of anti-resonant length. At anti-resonant lengths, for a given ultrasound wave, the peak-to-peak displacements at the distal end of the wire are at a local maximum. This ensures that, at the entry to a tapered section, the displacement wave is at a peak while the corresponding stress wave is at a local minimum. The effect of any stress concentrations at the taper points will therefore be lessened.

Anti-resonant lengths can be determined using an analytical equation, or, for complex geometries or where damping is significant, a finite element model. Anti-resonant lengths for a bar of uniform cross section with no damping can be determined using Equation 1. In this equation, $l$ are the anti-resonant lengths of the waveguide sections, $f_n$ is the frequency of the system (22.7 kHz in this case) and $c$ the speed of sound of the material (3410m/s).

$$l = \frac{nc}{4f_n} \qquad n = 2, 4, 6... \qquad \text{Equation 1}$$

Each of the tapered sections is to be one wavelength long, based on a frequency of 22.7 kHz (as determined using the laser sensor). This approach is intended to produce displacement anti-nodes (or local maxima) at the taper points. As the wavelength depends on the taper geometry, which is itself related to the length, an iterative design process must be used to determine the length of one wavelength in a tapered section.

### 3.3 Fabrication and Testing of Tapered Wire Waveguides

NiTi wires of 1.0 mm diameter, 2 metre length were tapered to the required dimensions using a grinding process. Ultrasound transmission tests were conducted by visual inspection of ablation of calcium carbonate specimens.

## 4. RESULTS

### 4.1 Laser Sensor Measurements

For the wire waveguide with a length of 278mm and 1.0 mm diameter, the distal tip displacement measurements for increasing input power dial settings, obtained using both the optical microscope and the laser sensor, are shown in Figure 3. Both sets of data show that as the power delivered from the generator is increased, the wire waveguide distal-tip displacements are also increased. This is not a linear relationship. As the value for the microscope is taken from a still image, a limited number of data points are available. The laser sensor data is presented in terms of an averaged value and standard deviation for each input power setting. The maximum standard deviation is 7%.

Transient frequency measurements of the same wire waveguide (length 278mm, diameter 1.0 mm) are shown in Figure 4. The results show that for low power settings, it can take approximately one minute for the device to settle at a specific frequency. However, as the power input from the generator increases, this settling time is decreased.

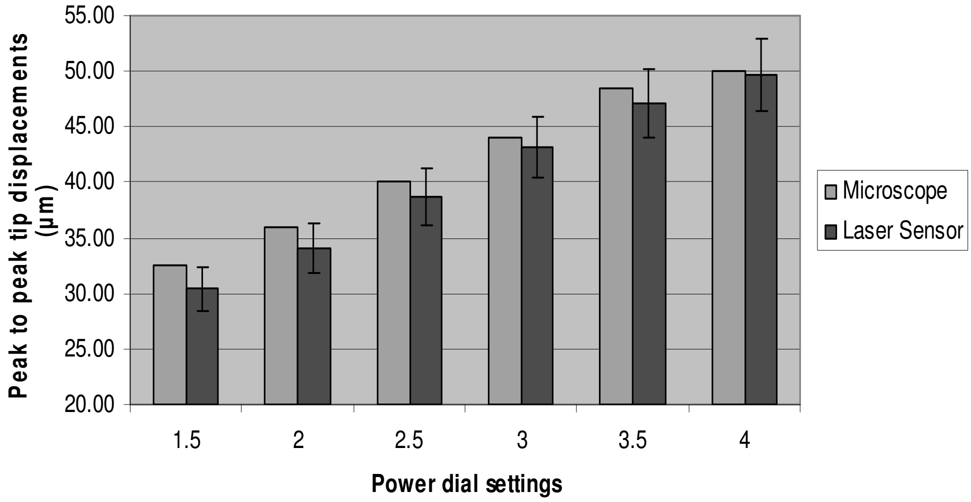


**Figure 3: Comparison of optical microscope and laser sensor for tip displacements with varying power dial settings**

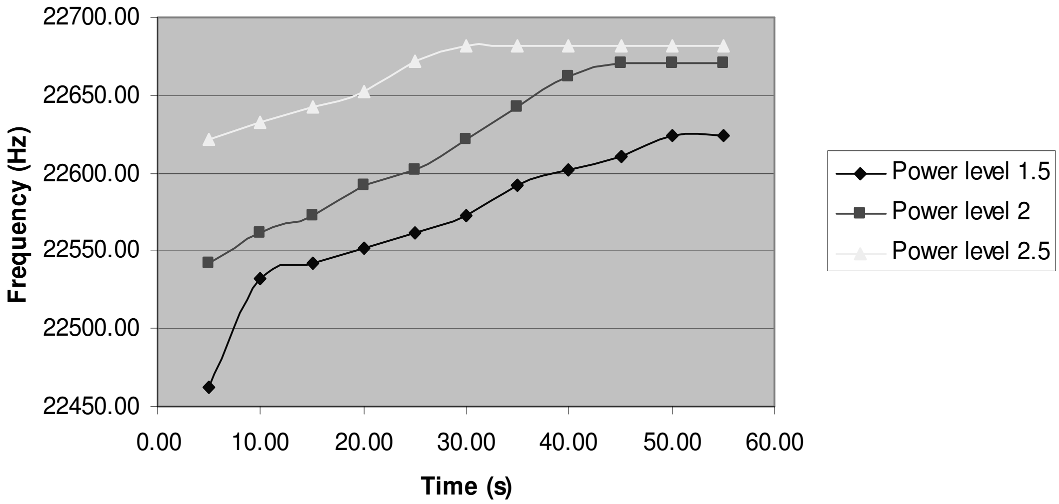


**Figure 4: Change in frequencies of the distal tip displacements**

The decrease in settling time may be due to the material characteristics of NiTi waveguides, as a result of fluctuations in temperature, frequency, amplitude, dynamic modulus, hysteresis and stress.

### 4.2 Waveguide design

Using the iterative finite element analysis procedure, lengths of 156.0mm and 153.5mm were determined for the 1.0 to 0.35mm and the 0.35-0.20mm one wavelength tapered sections respectively. Figure 5 shows the predicted amplification of the displacement standing wave along the length of the first taper (Section 2 in Figure 2).

To keep the length of Section 1 to a minimum, the anti-resonant length of 75.1mm (1/2 wavelength, $n = 2$) was chosen. The length of Section 3 was chosen so that overall length of the first three sections would be less than 1.4m. An anti-resonant length is again used to maximise amplitude transmission while minimising stresses at the taper points. A length of 1.05m (7 wavelengths) is selected. A length of 0.601m (4 wavelengths) was selected in order to achieve the overall length requirement, while maintaining an overall anti-resonant response for the tapered waveguide.

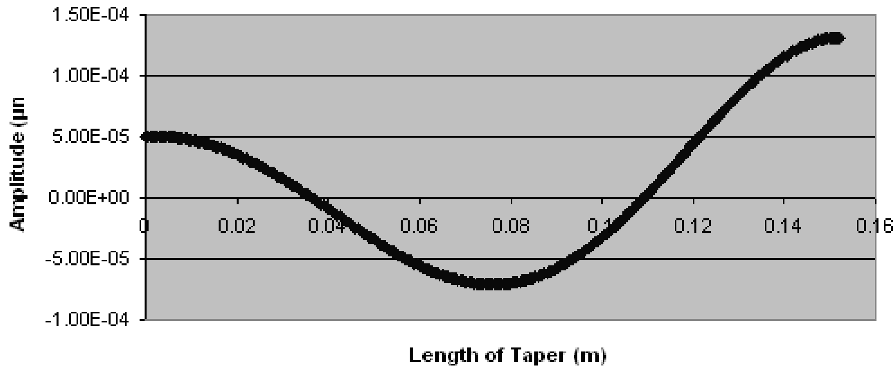


**Figure 5: Displacement standing wave of 1mm to 0.35mm tapered section**

Figure 6 shows the predicted standing wave internal displacements for the full tapered wire waveguide for a proximal input axial peak-to-peak displacement of 50µm.

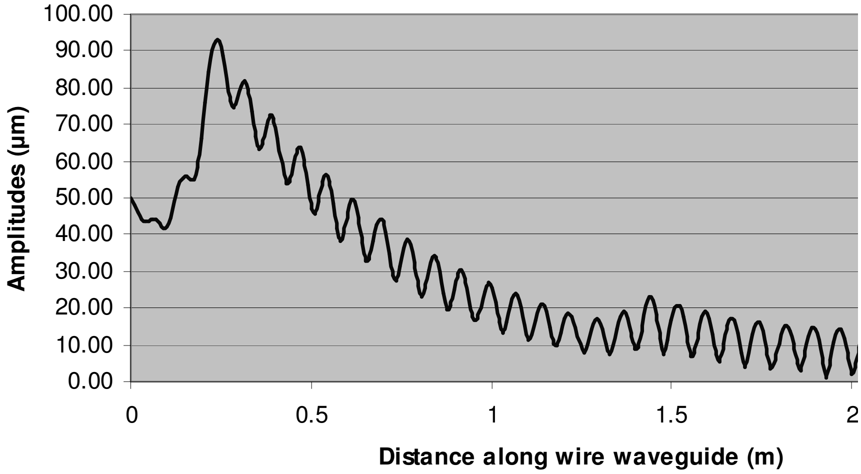


**Figure 6: Standing wave along length of tapered wire waveguide.**

A 4.5% damping value was used. Over long lengths (>1.5m) of wire waveguide with a damping ratio of 4.5% the predicted peak-to-peak distal tip displacements reduced from 50µm to less than 10µm. Damping at 4.5% is therefore predicted to significantly affect the strength of the ultrasound wave over a 2m length, and to overwhelm the amplification effect of the wire tapers.

### 4.3 Ablation Performance

For trials conducted with wire waveguide lengths in the 1587-1624mm and 1666-1697mm ranges, the tapered wire waveguide produced observable damage to the specimens at all lengths.

## CONCLUSIONS

The frequency output of short NiTi ultrasonic wire waveguides has been directly measured using a laser sensor. The sensor showed good agreement with the optical microscope measurement method (within ±5µm). The laser sensor measurements show that it can take up to a minute before the wire waveguide settles at a specific frequency and as the power dial settings are increased, the frequency also increases slightly.

A methodology for designing tapers in long wire waveguides has been presented. The effect of damping on the ultrasound wave is shown to be potentially problematic over long lengths, although this is somewhat ameliorated by the amplification provided by the wire tapers. Tapered wire waveguides with the required diameters and lengths have been constructed, and their ability to transmit high power, low frequency ultrasound at a level sufficient to ablate a model materials has been experimentally verified.


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