

Mechanisms of Ultrasonic Thrombolysis

Jeffrey J. Vaitekunas Ph.D, Elvira Lang M.D., Omnisonics Medical Technologies, Wilmington, MA USA and
Mark Schafer Ph.D., Sonic Tech Inc., Ambler PA, USA

Abstract

An ultrasonic transversely vibrating wire delivers energy to an active zone to facilitate thrombolysis in a blood vessel. Ultimately, all the energy delivered into the treatment region at the active zone ends up as heat. The heat created can originate from three sources. First, the stresses in the waveguide can create heat in the waveguide through internal frictional losses of the material. This heat is then conducted into the fluid surrounding the waveguide. The second source of heat generation is heating through absorption in the fluid due to the propagation of the acoustic field through the fluid. The third source of heating results from viscous losses as the wire moves through the fluid. This paper determines that the average power of an Omniwave ultrasonic thrombolysis system running in a single 20 kHz transverse mode with a 120 micrometer peak-to-peak amplitude is about 1.3 Watts due primarily to viscous losses.

Ultrasonic Thrombolysis

Figure 1 illustrates the Omnisonics Endovascular System that delivers energy to the active zone of its waveguide to enhance the infusion of physician specified fluids and to remove thrombus in the peripheral vasculature. The system used for this study consists of a transducer with an attached wire waveguide and a catheter covering the waveguide. The transducer converts a 40 kiloHertz electrical signal to ultrasonic energy transmitted longitudinally down the length of the wire waveguide. The catheter covers the wire waveguide to eliminate patient or physician contact along the longitudinally vibrating portion and to direct irrigation fluid along the length of the waveguide, cooling the waveguide. The waveguide distributes ultrasonic energy at its active distal section into 20 kiloHertz transverse waves that generate a beneficial clinical effect. The therapeutic ultrasonic energy is only delivered over the active distal section of the waveguide.

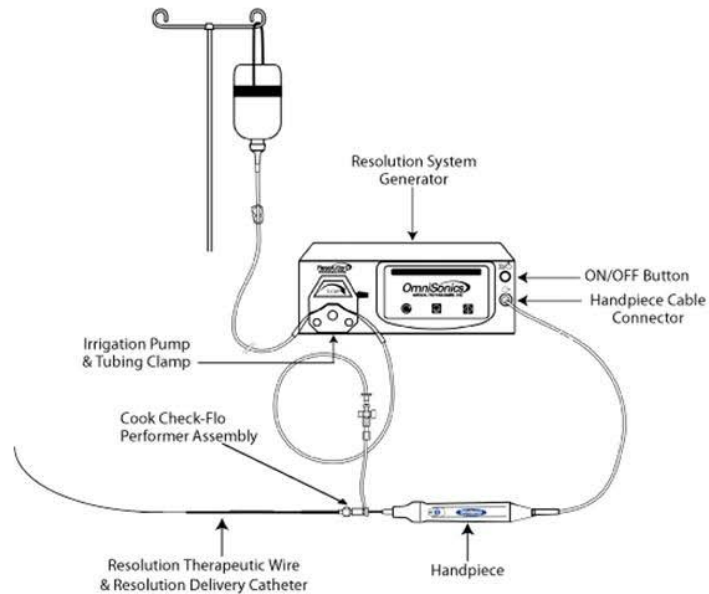


Figure 1. Ultrasonic Thrombolysis System

The system creates a standing transverse wave pattern at the distal section of a very small profile wire, designated as the waveguide. The transverse wave pattern creates ultrasonic energy circumferentially around the waveguide. By utilizing a transverse wave pattern, the system expands the “active section” from just the tip of a wire if vibrated longitudinally, to an active distal section when vibrated transversely. At the active section, the energy delivered creates several effects as illustrated in Figure 2. These include the ultrasonically induced primary mechanical mechanisms of: cavitation, microstreaming, and transverse motion, as well as secondary mechanisms such as microjet formation.

Omniwave Mechanisms of Action

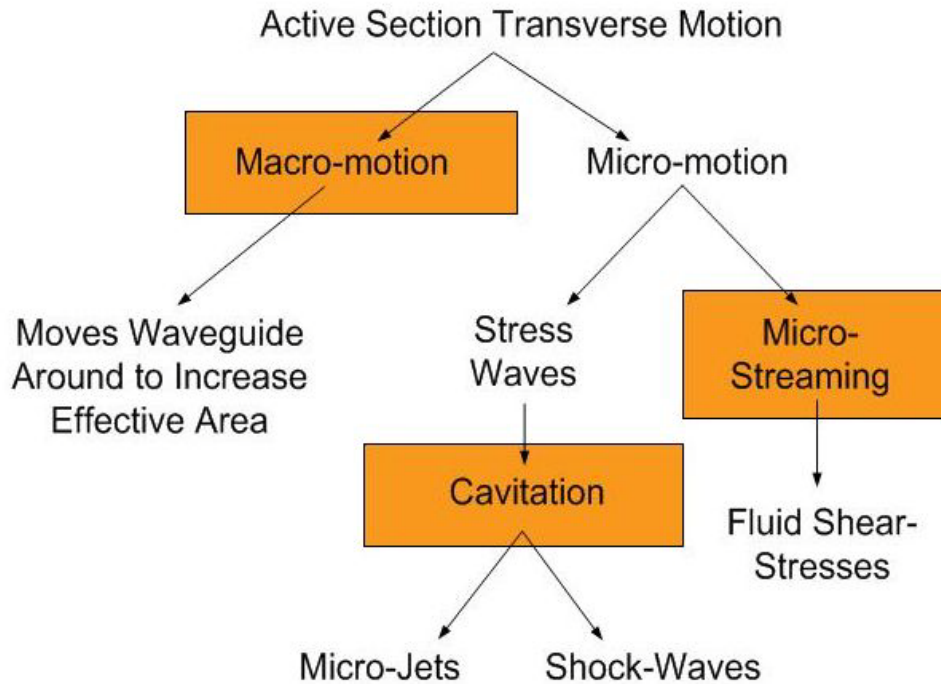


Figure 2. Ultrasonic transverse wire mechanisms of thrombolysis.

For example, in thrombolysis, the cavitation mechanism is known to contribute to breaking the fibrin strands that hold the thrombus together.^[1-4] Shear stresses from microstreaming and waveguide motion work in synergy with the cavitation mechanism to emulsify the thrombus. If fluids such as lytics are used, the microstreaming increases fluid flow and distribution of the lytic into the thrombus. These ultrasonic mechanisms of action selectively destroy fibrin without adversely affecting elastic tissues such as the vessel wall.¹⁻⁴ During thrombolysis, cavitation contributes to breaking the fibrin bonds that hold the thrombus together. Shear stresses from micro-streaming and the catheter system's macro-motion work in synergy with the cavitation mechanism to break up the thrombus. Macro-motion of the catheter system within the vessel also helps to expand the range of action to larger vessel diameters. These mechanisms work together to remove blood clots.^{5,6}

Mechanisms of Heating

The transverse motion of the waveguide at the active section also creates heat in the fluid within the vessel during treatment. The heat created can originate from three

sources. First, the stresses in the waveguide can create heat in the waveguide through internal frictional losses of the material. This heat is then conducted into the fluid surrounding the waveguide. This is analogous to the heating of a paperclip as it is repeatedly bent back and forth. This heating is significant when the material is plastically deformed, and is minimal when the material is elastically deformed. The Omniwave system's transverse active section is intentionally run in the elastic region. Due to the small level of strain in the active section of the Omniwave system, this heating mechanism is deemed insignificant relative to other mechanisms, and will be neglected in the present calculation.

The second source of heat generation is heating through absorption in the fluid due to the propagation of the acoustic field through the fluid. Absorption is a relaxation phenomenon that scales with frequency, and is often measured in dB/cm/MHz. A typical value for acoustic absorption in water is 0.3 dB/cm/MHz. Acoustic power output of the Omniwave system has been measured to be approximately 1 milliwatt or less.⁷ At the frequency of the Omniwave system, approximately 20 kHz in the active section, this heating mechanism should be at least an order of magnitude less than the third mechanism, viscous heating of the fluid. Therefore absorptive heating will also be neglected in the present determination of mechanisms of heating.

The third source of heating results from viscous losses as the wire moves through the fluid. As will be shown later, the Omniwave Endovascular system has a maximum Reynolds number of about 2000, which places the flow pattern consistent with pressure drag dominated flow. The Omniwave Waveguide has a circular cross-section, and therefore will be considered herein as a bluff body (not streamlined), and the viscous losses will be considered to be dominated by pressure drag. The waveguide displacement and velocity are varying sinusoidally, and therefore the Reynolds number is varying sinusoidally. Effectively, for computation purposes, the fluid flow with respect to the waveguide cross-section is varying sinusoidally. Further, the active section of the Omniwave waveguide exhibits a standing-wave pattern for the highest frequency components of vibration, experimentally determined at approximately 20 kilohertz for a 40 kilohertz transducer drive frequency. The transverse velocity of the active section is sinusoidally varying both in space and in time. Since the variation is sinusoidal, it is convenient to use RMS values to provide an effective velocity of the active section.

Calculation of the Viscous Losses

Therefore, based on the assumptions that pressure drag dominates the viscous losses and that RMS values may be used to approximate the effective velocities of the waveguide, the power of the Omniwave system required to overcome the viscous losses as the waveguide moves transversely through a fluid may be calculated as follows⁸:

$$Power = Force \cdot Velocity \quad (1)$$

The power of the Omniwave system required to overcome the viscous losses as the waveguide moves transversely through a fluid will be calculated from the Force exerted by Drag on the waveguide multiplied by the Velocity of the waveguide through the fluid. This calculated power is equivalent to the power from the Omniwave system dumped into heating the fluid that the system is immersed in as the waveguide vibrates within the fluid (using conservation of energy.) The force may be calculated as⁹:

$$Force = C_D \cdot \left[\frac{1}{2} \cdot \rho \cdot V^2 \cdot Area \right] \quad (2)$$

Where C_D is the drag coefficient, ρ is the density of the fluid, V is the velocity of the fluid with respect to the waveguide, and $Area$ is the projected area of the waveguide. For bluff bodies dominated by pressure drag the projected area is used instead of the surface area used for frictional drag of streamlined bodies.

$$Area = D \cdot l \quad (3)$$

Where D is the diameter of the waveguide's cross-section, and l is the length of the waveguide's active section. However, since there is a standing wave in the active section at 20 kilohertz, the amplitude of vibration is modulated as a function of position along the length of the waveguide. This variation is also sinusoidal, and therefore it is reasonable to take an RMS value for the length. Therefore the length l in the equation will be 0.707 times the actual length.

Plugging Equations 2 and 3 into Equation 1:

$$Power = C_D \left[\frac{1}{2} \cdot \rho \cdot D \cdot l \cdot V^2 \right] \cdot V = C_D \left[\frac{1}{2} \cdot \rho \cdot D \cdot l \cdot V^3 \right] \quad (4)$$

The average velocity, V , of a point (at the peak amplitude portion of the standing wave) on the waveguide with respect to time is the RMS velocity, which is:

$$V = 0.707 \cdot \omega \cdot Amp = 0.707 \cdot 2 \cdot \pi \cdot freq \cdot Amp \quad (5)$$

Where 0.707 is used to convert a sinusoidally varying signal to RMS, ω is the angular frequency, Amp is the zero to peak amplitude of the transverse vibration, and $freq$ is the cyclical frequency. So now the power may be written as:

$$Power = C_D \left[\frac{1}{2} \cdot \rho \cdot D \cdot l \cdot (0.707 \cdot 2 \cdot \pi \cdot freq \cdot Amp)^3 \right] \quad (6)$$

Calculation of the Power for a Single 20 kHz Vibration Mode

The Reynolds number is a function of fluid velocity with respect to the body, and the drag coefficient is a function of the Reynolds number, therefore the drag coefficient is a function of the fluid velocity. Since the fluid velocity with respect to the waveguide is varying sinusoidally, then the drag coefficient is also varying sinusoidally. The Reynolds number is defined as:

$$Re = \frac{\rho \cdot V \cdot D}{\mu} \quad (7)$$

Where ρ is the density of the fluid, V is the velocity, D is the diameter of the body, and μ is the dynamic viscosity. For water, μ is 10^{-3} kg/ms, and ρ is 1000 kg/m³. The maximum velocity of the 20 kilohertz transverse wave is 7.5 m/s at a 60 micron zero to peak amplitude and 20 kilohertz frequency, so the maximum Reynolds number is 1915. For a circular cylinder at a Reynolds number of 1915, the C_D is at a minimum 1, and increases as Reynolds number decreases, however it is relatively flat in the region of the Omniwave system's activity.

Equation 6 will be used to calculate the pressure drag related hydrodynamic power delivered by the Omniwave system. Specifically, the power from the 20 kilohertz component of the transverse active section will be assessed. The Omniwave system has an active section 0.010 inch in diameter, which when ultrasonically activated

exhibits a transverse standing wave pattern measuring 19 nodes with a node spacing of about 4.5 millimeters (corresponding to the 20 kHz driven mode of vibration.) This corresponds to approximately 10 full waves of transverse standing wave having an overall length of about 9 centimeters. So l will be taken as 0.707 times 0.09 meters = 0.06363 meters, D will be taken as 0.000254 meters, and $freq$ is 20,000 Hertz.

High speed camera measurements of the amplitude of the 20 kHz wave shape shows about 60 micrometers of amplitude, zero to peak, so Amp is taken as 0.00006 meters.¹ Water density is taken as 1000 kg/m³. Plugging these values into Equation 6 gives:

$$Power = 1.2 \cdot C_D \quad (8)$$

Therefore, since C_D has a minimum value of 1.0 for Reynolds numbers below 10⁴ for a circular cross-section body, the minimum power delivered from the current Omniwave system due to viscous losses from the single mode 20 kHz wave shape is 1.2 Watts. At a Reynolds number of 2000, which is the Reynolds number for the RMS velocity of the Omniwave system, the C_D has a value of about 1.1. Therefore the average power of an Omniwave system running in a single 20 kHz transverse mode with 120 micrometers peak-to-peak amplitude is about 1.3 Watts.

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¹ Transverse amplitude measurements are taken from Omnisonics' internal archive document A00249, page 11, GLP No-Balloon Waveguide Kit A3 Micromotion Evaluation.