Liquid Core Light Guide for Laser Angioplasty

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INTRODUCTION

TECHNICAL demands for laser angioplasty catheters, particularly for destinations in coronary arteries are in general, more stringent than those for angiography and balloon angioplasty. Catheters for laser angioplasty must be flexible and atraumatic in order to safely negotiate the angles of curvature encountered within tortuous and stenotic vascular lumens while being rugged, mechanically and optically. Optimally, laser catheters would be compatible with conventional catheterization and guidewire techniques to guide them to distal vessels via manipulation from percutaneous sites. Once maneuvered to the desired irradiation site, precise laser energy exposure to the pathologic tissues is required without interference from blood or ablated debris. An adequate volume of tissue must be removed to make the procedure worthwhile while incurring minimal damage to surrounding structures. Thrombosis, vasospasm, or perforation of the vessels must be avoided, while providing a favorable substrate for vascular healing. Thus far, catheter designers have utilized fused silica fibers to transmit the laser energy. While integrating these fused silica fibers into catheters is possible, it can be complex, expensive, and sometimes limited by stiffness imposed by the silica fibers. We sought to find a simple, inexpensive alternative to fused silica fibers which might provide superior catheter characteristics.

Optically-transparent fluid was studied as a means of transmitting energy in a laser angioplasty catheter and the performance of a fluid-core catheter for removing coronary artery obstructions was evaluated.

Fluid-core optical transmission devices have been used primarily for industrial applications where flexibility, cost, and high optical throughput are considerations. Medical applications of these devices have been scant. In one report, Sander describes guiding Nd: YAG laser energy through a stream of water utilizing the difference in indexes of refraction between water and air to carry infrared light short distances from fiber tips to treat tumors in the rectum and stomach [4].

DESIGN CONSIDERATIONS

Optics

Fluid-core light guides operate by the same principles as solid-core optical fibers. Light transmitted through the lower index-of-refraction core is totally internally reflected from a higher index-of-refraction cladding material when incident at an angle greater than a critical angle $d$ given by

$$\sin d = \frac{n_2}{n_1}$$

where $n_1$ and $n_2$ are the indexes of core and cladding, respectively. (Fig. 1). Increasing the difference in index of refraction between core and cladding therefore maximizes the angle at which off-axis rays can be conducted in the core and minimizes losses arising from bends, for example, in tortuous arteries. In addition, for optimal light transmission, the interface between the core and cladding must be smooth and uniform. Both the core and the cladding material must withstand the optical intensities used, and neither should have appreciable optical absorption or scattering.

Optical Core Fluid

Optical transmission fluids for use in a catheter assembly must be transparent to applicable laser wavelengths and have the high index of refraction necessary to allow appropriate light transmission as well as be suitably nontoxic for intravascular use. Of the transparent fluids which are used routinely for intravascular injection, few will suffice as an optical transmission medium. Radio-opaque dyes are usually water soluble salts of tri-iodinated, substituted benzoic acids which are injected to temporarily replace blood and opacify the vessel to be imaged radiographically. These dyes are high viscosity, high osmolality fluids which are nearly 100% transparent in the visible spectrum. Angiography involves the injection of these agents into the desired vessel and simultaneously obtaining X-ray images on film or videotape. The use of iodinated contrast media or radio-opaque dyes as an optical transmission fluid would therefore be additionally advantageous from an imaging standpoint.

Optical Catheter Cladding

Cladding for a fluid-core laser catheter must be biocompatible for intravascular use and have optical stability with minimal light absorption within the waveband of laser emission. Because of high optical powers to be used and the generation of tissue heating near the catheter tip, a

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material which is nonflammable and thermally stable with a high melting point would be advantageous. The cladding functions as an integral part of the catheter and therefore must not add unwanted physical characteristics to the system.

**Catheter Assembly**

The use of fluid optical transmission can increase flexibility of laser catheters and allow a wide range of catheter diameters to be employed without causing stiffness. Initial prototypes consisted of an optical fluid encased in a low-index-of-refraction tubing which was terminated at both ends in various configurations of fused silica end windows. These sealed liquid light guides were highly flexible in comparison to fused silica fibers; however, direct catheter contact with target tissues was required secondary to the confounding effects due to blood intervening between the catheter and tissue.

To solve this problem, the distal end window can be eliminated and a flowing optical transmission fluid can be used to flush blood from the laser field. A stream of high-index-of-refraction optical fluid in the vessel can act as a crude optical guide over short distances because blood, with a relatively low index of refraction \((n_d = 1.34-1.36)\) can act as an optical cladding material. The process of internal reflection can then continue from the end hole of the catheter to the target. If an atraumatic fluid stream is created, contact between the catheter tip and tissue is no longer necessary and an atraumatic, noncontact means of delivering laser energy may result. When a radio-opaque fluid is used as the optical transmission fluid, the catheter, the site of laser energy delivery, and the distal vessel can be visualized while the laser is fired. Without an end window, the central fluid channel is also available for guide-wires or other devices when it is not being used for optical transmission.

**Laser Catheter Coupling**

With respect to launching the laser light into a fluid-core optical catheter, a glass or fused silica window may be placed in the proximal end of the catheter, through which laser light can be transmitted. These windows, however, would require highly accurate manufacturing, would fix the location of the laser end of the catheter, and necessitate either a long catheter or placement of the laser nearer the patient. In order to locate the laser a convenient distance from the patient and to reduce the complexity and expense of an optical window in the catheter, the laser can be coupled to a standard fused silica fiber which transports light to the optical fluid catheter. The fiber can be introduced via an O-ring connector and advanced within the core fluid itself to the body of the catheter, thereby preserving flexibility in the distal portion. If a silica fiber is used for coupling, the refractive index of the optical fluid and the coupling fiber should be closely matched to reduce reflective losses.

**Optical Fluid Flow**

An ideal optical fluid injection will produce the least turbulence in the stream of optical transmission fluid while having nominal and well-controlled jet energy at the exit point of the catheter to minimize jet-induced vascular damage. The stream must also have enough kinetic energy to maintain a discrete stream to carry the light effectively to the intravascular target.

**MATERIALS AND METHODS**

**Optical Core Fluid**

Angiovist 370 (Berlex Labs, Wayne, NJ), Renographin 76, Hexabrix (Malinkrodt, St. Louis, MI), and a 50:50 Angiovist/0.9 normal saline mixture were evaluated as optical core fluids. We examined transmission spectra of fluids using a Hewlett-Packard Model 8452A spectrophotometer (Hewlett-Packard, Andover, MA). A Milton-Roy Model 39-45-03 Refractometer (Milton-Roy, Rochester, NY) was used to measure the refractive index of iodinated contrast solutions \((n_1)\) and blood \((n_3)\) at 20°C. *In vitro* and *in vivo* studies were performed with Angiovist 370 and Hexabrix solutions.

**Optical Cladding**

Teflon FEP (Dupont) was chosen as the optical cladding material with an index of refraction \((n_2)\) of 1.338. The numerical aperture of the catheter was calculated to be 0.51 with a 23° acceptance angle. This material was extruded in a tube with an inside diameter of 1.1 mm.

**Catheter**

The catheter assembly was composed of a Teflon inner core with a laminated wire braid added for torsional control (see Fig. 2). The proximal catheter ends in a hub to which is attached a Touhey Borst O ring and Y adapter (USCI, Billerica, MA). The 400 µm core diameter silica coupling fiber was advanced into the catheter through the
O ring in the Y adapter, which prevented egress of the optical core fluid. The luer-lock portion of the Y adapter was attached to a power injector via an injector hose. The catheter was then filled with contrast material with care to exclude all air bubbles.

Injector and Flow Rates

We used Angiomat 3000 and Med Rad Mark 5 (Medrad Inc., Pittsburgh, PA) injectors operating at maximum pressure cutoffs of 150-300 lb/in². Flow rates of 0.3-0.5 cm³/s were used for 5 and 10 s injections, which resulted in 1.5 to 5.0 cm³ injection volumes.

Laser

A Candela MDL 100 or a Dymed Model 3000 flash-lamp-pumped dye laser operating with 1-10 μs (FWHM) pulsewidths was used. The laser excited coumarin dyes (Exiton) to produce 480 nm radiation at energies up to 500 mJ per pulse at 2-10 Hz. The lasers were coupled via a 50 mm fused silica lens to a 400 μm fused silica optical fiber (Polymicro Technologies Inc., Phoenix, AZ). Direct laser power output was measured with a Scientec 365 meter.

Optical Measurements

A Scientec power meter was used to measure pulse energy at the laser, through the coupling fiber, and through the entire device. The optical fiber was inserted into the laser catheter via an O-ring Y adapter (USCI Billerica, MA) and positioned 10 cm from the end hole. Output energy from the stream of optical transmission fluid in a glass beaker of water or blood was measured by positioning the power meter below the beaker, as shown in Fig. 3. The end hole of the catheter was positioned approximately 1 cm from the bottom of the beaker and the stream directed vertically downward. To reduce confounding reflection losses in determining transmission efficiencies, optical fiber outputs were also measured similarly to the laser catheter held 1 cm from the bottom of the beaker. Transmission efficiency was determined as a ratio of the measured output between the catheter assembly and the optical fiber.

In Vivo Studies

In order to test the feasibility of this catheter system for coronary artery applications, we created thrombotic occlusions in the proximal left circumflex coronary arteries of dogs. A stenosis distal to the coronary artery occlusion was created by an externally-placed plastic band [3], [4]. This model is illustrated in Fig. 4. 2 h after the thrombotic occlusion was created, the fluid laser catheter was introduced from a femoral or carotid artery cannulation and delivered to the circumflex artery via an 8f angioplasty guiding catheter (Interventional Medical, Hanover, MA) placed in the ostium of the left main coronary artery. The laser catheter was advanced to the circumflex coronary artery via the guiding catheter under fluoroscopic control with the laser catheter prefilled with iodinated contrast media (Angiovist or Hexabrix). The catheter was maneuvered to the circumflex artery over a leading 0.018 in an-
gioplasty guidewire. In some cases, it was possible to maneuver the catheter into the artery simply by applying torque to the proximal portion of the catheter. When the catheter tip was positioned just proximal to the occlusion, the injector initiated contrast flow at 0.3–0.5 cm³/s for two 10 s intervals in 13 animals to determine the hydraulic effect of the fluid stream. Five 10 s duration streams of contrast were then injected at 0.3–0.5 cm³/s and once the contrast was seen fluoroscopically exiting the end hole of the laser catheter, the laser was activated at 3–10 Hz. Laser energy was delivered via the 400 μm diameter optical fiber at 40 to 80 mJ per pulse, which resulted in fluences of 3.0 to 7.5 J/cm² at the exit hole of the laser catheter. While the laser was firing, the stream of contrast was radiographically imaged and recorded on 35 mm film and videotape. The laser catheter was advanced or repositioned within the lumen and the laser reactivated until the occlusion was completely removed and distal perfusion established.

RESULTS

Optical Fluid Measurements

Transmission spectra of Hexabrix for a standard 1 cm pathlength cuvette, against water as a reference, are presented in Fig. 5. Iodinated contrast media were found to have an index of refraction of 1.46 at 26°C. Table I shows indexes of refraction of contrast media and other fluids tested.

Catheter Performance

Due to the large difference in the indexes of refraction between water and iodinated contrast media, the stream of contrast was easily visualized when injected into a body of water. At different flow rates and driving pressures, differences in the nature of the flow pattern exiting the end of the catheter was observed. We found that flow rates between 0.2 and 0.5 cm³/s would create a discrete stream which would not disperse for a length of 1 cm. These injection rates produced catheter flow well below the threshold for full turbulent flow at the exit hole of the catheter with Reynolds numbers between 60 and 94. When a discrete stream was obtained, energy transmission in excess of 70% was observed over stream distances of 1 cm. When measured beyond a point in the stream where dispersion from turbulence has occurred, there was negligible energy transmission.

Pulse energy was measured through a 10 cm length of fluid catheter, using a Teflon FEP as the cladding and iodinated contrast media as the optical transmission fluid pumped at 0.3 cm³/s via a Med Rad injector. No difference in energy transmission was found when 90° bends with a 2 cm radius of curvature were placed in the distal portion of the fluid-core catheter. With the end hole of the catheter positioned 1 cm from the wall of the beaker of water, the maximum output of the laser (500 mJ per pulse at 480 nm) in 10 μs pulses at 3 Hz was launched into the flowing stream of contrast media without visible damage to the catheter. An average of 400 mJ/pulse was observed. The catheter transmission efficiency is, therefore, 80%. Fig. 6 shows a photograph of a fluid-core optical catheter transmitting a 1 μs laser pulse to a Teflon target in a water bath.

Air bubbles introduced within the fluid-core system resulted in dramatically reduced transmission efficiency. Air bubbles, with an index of refraction of 1.0, were highly reflective and were easily located visually as bright spots within the tubing. With bubbles within the catheter during transmission of high-power laser pulses, focal catheter damage occasionally occurred. Teflon degradation ranged from etching or darkening of the inner catheter surface to softening and loss of structural integrity. Once the Teflon surface was damaged, catheter light transmission was low and further laser pulses were apparently absorbed, increasing catheter damage. Air bubbles not expelled during the initial filling of the catheter with contrast media and adherent to the Teflon tubing resulted in most of the observed catheter damage, whereas bubbles which were introduced and flowed down the catheter only resulted in transient loss of energy transmission.

Tight kinking (folding) of the catheter resulted in similar damage to the catheter. Kinking results in angles of incidence much less than the critical angle for internal re-
reflection at the catheter cladding and therefore, light is transmitted into the catheter. Laser energy directed at the Teflon FEP in a bath of contrast media placed at an incident angle of 90° resulted in plumes of black material and visible damage to the catheter. In this instance, laser-induced damage began with focal absorption in the Teflon. We examined catheter failure points using a Wild stereodissecting microscope. The initial damage appears as darkening of the catheter surface. With further pulses, microbubbles appear in the substance of the Teflon wall. If laser pulses were continued to be applied, this process progressed to loss of structural integrity and weakness at the absorption point. Ultimately, catheter perforation and melting occurred.

Animal Trial

A catheter inside diameter of 1.06 mm and an injection rate of 0.3-0.5 cm³/s produced a stream of fluid which provided adequate opacification of canine coronary arteries during fluoroscopy and a stream capable of effectively delivering high-peak-power laser pulses to intravascular targets. Injection flow rates between 0.5-1.0 cm³/s tended to produce unwanted hydraulic effects during ablation of target tissues in vivo. While these flow rates did not produce overt trauma to the vessel, ablation debris was occasionally flushed retrograde in the vessel and subsequently embolized to the systemic circulation.

In no instance did the occlusion resolve or change with fluid injection alone nor was angiographic evidence of vascular injury observed. In no case did catheter kinking occur. All catheters were inspected for damage. In only one case was there evidence of laser catheter damage. In this case the laser was fired inadvertently without a flowing stream of contrast. Blood had displaced contrast media within the tip of the catheter. Upon visual inspection, the tip of the catheter had blackened, presumably either from detonation of blood elements or light-induced etching of the Teflon surface. There was no gross evidence of structural damage or catheter compromise.

An audible popping sound was routinely heard emanating from the chest wall during laser activation when the energy was directed at the thrombotic occlusion. Since the laser energy was transmitted through a stream of radiopaque contrast media, the laser catheter and coronary artery could be seen at all times during the laser activation and thrombus removal could be visualized as it occurred. All occlusions in all animals treated with laser energy were completely removed within 100 s, with the majority of occlusions being removed with less than 30 s of laser energy delivery. A coronary angiogram showing left circumflex artery occlusion before laser treatment is shown in Fig. 7(a). Fig. 7(b) is an angiogram following laser treatment demonstrating complete removal of the coronary artery thrombus with a residual angiographic defect caused by the external band stenosis. There were no perforations, vasospasms, or other acute, untoward effects.

DISCUSSION

This study shows that a relatively simple flowing, fluid-core laser angioplasty catheter can eliminate many of the
Fig. 7. (a) Angiogram of a canine coronary artery showing a complete thrombotic obstruction of the left circumflex coronary artery at the closed arrow. (b) Angiogram of the canine coronary artery following laser treatment with a fluid-core optical catheter showing complete removal of the thrombus and the residual 90% stenosis (open arrow) created by a fixed external plastic band. There is no evidence of perforation or other damage.
design constraints imposed by fused silica fibers. With liquid-core optical fibers, flexibility is limited only by the cladding material, therefore, the area of tissue irradiation can be based on optimal light–tissue interactions rather than on constraints of catheter flexibility imposed by fused silica fibers.

We investigated cladding materials and found Teflon FEP (Dupont) which has a low index of refraction (1.338) and is an extrudable, low-cost material which is biocompatible. This compound has an extremely low coefficient of friction which enables smooth intraluminal passage of guidewires or optical fibers and has the benefit of having extensive previous utilization in intravascular and other medical applications. Teflon FEP is almost inert to intravascular materials, has a very high melting temperature (360°C), and is inflammable.

The optical transmission fluid flushes away highly-absorbing blood while allowing a noncontact, atraumatic delivery of laser energy to the tissues. A fluid-core angioplasty catheter using radio-opaque contrast media as the optical transmission fluid core can offer catheter, target, and distal vessel visualization during laser activation. We found that conventional iodinated contrast used routinely in angiography is relatively nontoxic, transparent in visible wavelengths, and can transmit ablative high-power laser pulses efficiently without optical breakdown. All radiographic contrast agents absorb strongly in ultraviolet wavelengths and, therefore, would be unsuitable for transmitting ultraviolet light generated by excimer lasers now being utilized in clinical trials. It is also unlikely, considering the water content of these dyes, that transmission of high-power-pulse energies from holmium or erbium: YAG lasers would be feasible.

Angiographically, the ablation of intravascular obstructions described in this paper appeared to occur at the interface between the thrombus and the stream of optical fluid exiting the catheter. It was not necessary to directly appose the catheter against the thrombus. Since blood has a relatively low index of refraction (approximately 1.34–1.36, depending upon plasma constituents), it is possible that internal reflection at the blood–fluid boundary layer helps guide transmitted energy to the thrombus. However, because of high absorption and scattering, blood is far from an ideal cladding material. While these losses would frustrate light transmission over larger distances, this study shows that adequate transmission efficiencies can be achieved in distances relevant to laser angioplasty.

From in vitro observations, the point beyond the catheter where turbulent mixing of the optical fluid stream begins, is where effective light transmission ends. Mixing the optical fluid with blood not only alters the favorable ratio of indexes of refraction but also leads to absorptive events and scattering losses from blood constituents.

Optimal forward light transmission also involves an optical fluid stream with predominantly laminar flow such that stream lines of the fluid will remain intact. Conditions of flow velocity, vessel diameters, and fluid viscosities and densities determine laminar versus turbulent flow, and are related to the Reynolds number. The Reynolds number ($N_{Re}$), a dimensionless number, reduced to its simplest form is

$$N_{Re} = \frac{D V \rho}{\mu}.$$  

In this paper, $D$ = vessel diameter (0.11 cm), $V$ = flow (cm/s) $0.5 \text{ cm}^3/\text{s} = 52.6 \text{ cm/s}$, $0.3 \text{ cm}^3/\text{s} = 31.3 \text{ cm/s}$, based on an area of 0.95 mm$^2$ or 0.0095 cm$^2$, $\rho$ = fluid density (g/cm$^3$), and $\mu$ = viscosity (g/cm $\cdot$ s).

Reynolds numbers, depending on vessel and catheter exit hole geometry, between 2000 and 3000 generally have a completely turbulent flow at the exit point of the catheter, between 2000 and 77 have transitional flow patterns which are part turbulent and part laminar, and below the critical number of 77, are entirely laminar. The Reynolds number for flow rates of 0.3 and 0.5 at 37°C for these experiments were 60 and 94.

An optical fluid with a higher viscosity than ambient fluid would potentially diminish mixing and therefore maintain integrity of the stream, especially in laminar flow conditions. Contrast media have viscosity ratings between 8.9 and 10.6 centipoise [mg/cm (s)] at 37°C. High viscosity is generally felt to be undesirable in routine angiography injections as it increases the resistance to flow during injections through small bore catheters. However, for the purpose of displacing blood and maintaining an intact column or stream of transparent fluid beyond the distal tip of the catheter to conduct light in a blood stream, a high viscosity is desirable since it can provide high shear forces between the contrast media and lower viscosity blood to maintain the integrity of the stream.

Initial studies utilizing a flowing optical transmission fluid entailed hand-injection of the optical transmission fluid. Due to the high viscosity of iodinated contrast media and to small diameter laser catheters whose lumens were partially filled with either a guidewire or optical fiber, high resistances to flow were encountered. Fortunately, substantial experience has accumulated with controlled injection of angiographic fluids using high-pressure injectors whose flow, volumes, and pressures are carefully regulated over a large range to minimize intravascular trauma. The low flow stream of optical transmission fluid needed for the fluid-core laser catheters are fully within the technical capabilities of these machines. Injection equipment, currently in place in angiography suites, therefore, appears to be adequate for this application.

Coupling the laser energy into the fluid-core catheter was accomplished simply and inexpensively with readily-available silica fiber without adding stiffness to the portion of the catheter which must traverse the coronary vasculature. The fluid channel functioned easily as a course for guidewires and other devices and the catheter as a whole was easily integrated into standard angioplasty catheter systems. Thus, many design requirements were addressed with the use of flowing fluid-core optical catheters, while simultaneously reducing complexity and expense over solid optical fiber catheter designs.

Disadvantages to such a system for intravascular application were observed during development and feasibility testing. Intentional kinking of the fluid catheter compromised laser energy transmission and resulted in significant
structural damage to the system. Supporting the Teflon lumen with other plastics and ensuring an optimal catheter wall thickness-to-lumen ratio may reduce the possibility of kinking of the cladding. Delivery of the fluid catheter over conventional angioplasty guidewires further reduced the probability of kinking. Using these techniques in this study, catheter kinking did not occur during feasibility testing in 26 canine coronary vessels. The possibility of catheter kinking or other failure modes can probably not be completely eliminated, and detection of such events with subsequent feedback deactivation of the laser may ultimately be desirable.

The introduction of air bubbles into catheters during intravascular procedures is always scrupulously avoided. An airtight system from injector reservoir to the end hole of the catheter was utilized during the canine feasibility trial (Fig. 2), which resulted in no observable evidence of catheter damage attributable to air bubbles. Scrupulous removal of air bubbles during filling of the catheter and confirmation by observing the system with the simmer beam of the laser directed through the column of fluid to check for point reflectance may have contributed to the absence of this phenomenon. Air bubbles introduced during filling of the catheter with fluid tended to adhere to the catheter wall whereas air or particulate material introduced subsequently, tended to flow through the catheter and act less as a constant point source of reflection into the catheter, thereby potentially reducing the chance for significant catheter damage.

While kinking of the catheter and optical transmission fluid impurities were not evident in 26 canine coronary laser angioplasties, in one instance, the laser was inadvertently fired while blood had refluxed back into the catheter. This event created what appeared to be minor damage at the tip of the device. This can be prevented by firing the laser only during fluid injection periods, which is confirmed by fluoroscopy.

CONCLUSIONS

Delivery of laser energy to intravascular targets through a flowing fluid-core laser angioplasty catheter offers new design possibilities and solutions to current practical problems facing laser angioplasty. Fluid-core catheters using iodinated radiographic contrast material as the core fluid can transmit high-peak-power visible laser pulses at high efficiencies while offering improved imaging of the target and distal vasculature. These catheters are simple to produce, are optically and mechanically stable, and are compatible with conventional angioplasty equipment and techniques.

In canine coronary arteries in vivo, the catheters proved to be flexible, atraumatic, and able to deliver ablative high-peak-power laser pulses. With proper development, flowing fluid-core optical catheters may offer a superior alternative to silica fiber-based laser angioplasty catheters.

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