Laser Micromachining for Biomedical Applications

Philip R. Miller, Ravi Aggarwal, Anand Doraiswamy, Yi Jen Lin, Yuan-Shin Lee, and Roger J. Narayan

Laser micromachining is becoming a common method for fabrication of microstructured medical devices. Developments in pulsed laser technology have made it possible to achieve precision machining of sub-micrometer features with minimal damage to the surrounding material. Several aspects of laser micromachining, including machining methods, types of lasers used in micromachining, and laser-material interaction, are discussed in this article. Biomedical applications of laser micromachining are also reviewed. The ablation behavior of silicon was examined as a function of laser energy, aperture, and repetition rate. In vitro studies showed that microscale grooves on silicon substrates may be used to orient human aortic vascular smooth muscle cells. We anticipate that the use of laser micromachining for modifying medical and dental devices will become more significant over the coming years.

INTRODUCTION

The field of laser science has developed very rapidly over the past 40 years. For example, advances in laser technology have enabled the use of lasers for micromachining of materials used in automotive, aerospace, machine tool, microelectronic, and biomedical devices. The term laser micromachining refers to the use of lasers for cutting, drilling, welding or other modification of a material in order to achieve features on the single-digit or double-digit micrometer regime. Laser micromachining methods can be broadly organized into three categories: direct writing, mask projection, and interference.[1] In direct writing, the laser beam is focused on the substrate and the desired pattern is fabricated either by translating the laser beam or by translating the substrate. The important parameters in direct writing techniques include the working distance, the size of the focal point, and the depth of focus. This technique can be integrated with computer-aided design software and micropositioning equipment in order to enable automated movement of the substrate or the laser beam. The direct writing method may be utilized for cutting, drilling, or scribing a material. The mask projection technique involves the use of a laser to illuminate a given feature on a mask, which is projected to a much smaller size on the substrate. This method enables fabrication of large patterns on the substrate using a relatively low number of laser pulses. The resolution of features created using this technique is determined by the mask and the projection system. The technique requires the laser beam to be homogenous in order to achieve the same intensity of the laser beam over the entire mask area. The interference technique involves splitting the primary laser beam into two beams, which are superimposed in order to create an interference pattern. The interference pattern is projected on the substrate and the micromachined pattern corresponds with the intensity profile of the interference pattern.

Lasers can operate in either the continuous wave mode or the pulsed mode. In the continuous wave mode, laser output is essentially constant with time. On the other hand, the laser output is concentrated in small pulses in pulsed mode. An important task in laser micromachining is minimizing heat transport to the region of the substrate that is immediately adjacent to the micromachined material. This task is often achieved using a pulsed laser; these devices provide pulses with sufficient energy for micromachining a given material and small pulse durations for minimizing heat flow to surrounding material. The length of a laser pulse can vary from milliseconds to femtoseconds. In most cases, the peak power of the laser is inversely correlated with the duration

How would you…

…describe the overall significance of this paper?

Laser micromachining is a very useful technique for fabrication of stents, catheters, MEMS, microfluidic devices. The effects of aperture size, laser energy, and repetition on ArF excimer laser ablation of silicon wafers are described. Microscale grooves on silicon substrates facilitated orientation of aortic vascular smooth muscle cells.

…describe this work to a materials science and engineering professional with no experience in your technical specialty?

Laser micromachining is becoming a common method for fabrication of microstructured medical devices. Excimer laser micromachining of microscale grooves on silicon (111) wafers is discussed. The ablation behavior of silicon is examined as a function of laser energy, aperture, and repetition rate. Microscale grooves on silicon substrates may be used to orient human aortic vascular smooth muscle cells.

…describe this work to a layperson?

There have been many recent advances in the development of microstructured biomedical devices for use in minimally invasive surgery and other advanced surgical techniques. The complexity and small feature sizes required in these devices necessitates the use of laser micromachining and other advanced micromachining techniques. We anticipate that the use of laser micromachining for modifying medical and dental devices will become more significant over the coming years.

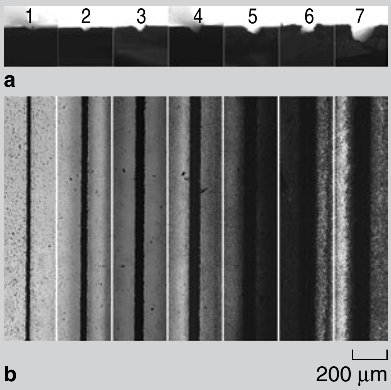

Figure 1. An optical micrographs showing ArF laser micromachining of Si (111) as a function of aperture. (a) Cross-sectional view, (b) top-view.

of the laser pulse. Hence, pulsed lasers can attain much higher peak power values than continuous wave lasers. A wide variety of lasers, which provide wavelengths from ultraviolet to infrared, may be used for micromachining. Excimer lasers typically function at 157 nm, 193 nm, 248 nm, 308 nm, or 351 nm; the emission wavelength depends on the composition of the gas that is used in the laser cavity. Excimer lasers are suitable for processing a wide range of materials due to the fact that these devices provide high energy photons. Most materials strongly absorb ultraviolet wavelengths; as a result, excimer lasers provide both low machining rates and high machining precision. Diode-pumped solid state (DPSS) lasers utilizing Nd:YAG emission in the third (355 nm) and fourth harmonic (266 nm) are also employed in laser micromachining. Due to the fact that DPSS lasers are highly coherent, these devices can be used to process very narrow spots. Ti:sapphire solid state lasers (700 nm–1,100 nm) are also employed in micromachining applications. Carbon dioxide gas lasers (10,600 nm) have found limited roles in micromachining applications because the smallest achievable spot size is ~50–75 µm. CO_2 laser are typically utilized in roles where low operating costs and high throughput are determining factors. The type of laser employed for a given micromachining application is determined by the substrate material and the dimensions of the micromachined feature(s).

Laser machining primarily involves laser-material interaction leading to ablation of the substrate material; removal of material occurs when the laser transfers energy in excess of the binding energy of the substrate material. The mechanism of energy transfer is dependent on material properties as well as laser properties, including pulse width, peak power, and emission wavelength. Materials may also absorb laser energy either by thermal or/and photochemical processes.[2] In thermal ablation, absorption of laser energy causes rapid heating, which results in melting and/or vaporization of the material. The thermal ablation process may be associated with a large heat-affected zone. Thermal ablation is commonly observed with long wavelength and continuous wave lasers (e.g., CO_2 lasers). Photochemical processes are observed when the laser photon energy is greater than the bond energy of the substrate material. In this case, the substrate material is vaporized because of bond dissociation that is induced by photon absorption. Thermal effects do not play a significant role in photochemical processes. This ablation mechanism plays a significant role in ultraviolet excimer laser-based machining. Laser ablation of materials demonstrates threshold behavior in that ablation takes place when laser fluence (energy per unit area) exceeds a minimum value. This threshold is a function of laser properties (e.g., emission wavelength and pulse width) as well as material properties. The threshold for laser ablation depends strongly on the optical properties (e.g., the absorption coefficient [α]) and the thermal properties (e.g., the thermal diffusivity [κ]) of the substrate material.[1] The laser ablation process is more efficient if the substrate material is able to absorb higher amounts of laser energy. A decrease in thermal diffusivity of the substrate material is associated with less rapid heat dissipation to surrounding material and an increase in ablation efficiency. Pulse duration is another parameter that can have a significant effect on the laser-material interaction. Materials processed using lasers with short pulse durations exhibit smaller heat-affected zones than materials processed using lasers with long pulse durations since less time is available for thermal diffusion to surrounding material. The desire to reduce laser pulse duration has motivated the development of ultrashort pulse lasers (e.g., femtosecond lasers). It should be noted that laser-material interactions in femtosecond lasers are fundamentally different than laser-material interactions in lasers with longer pulse durations. Femtosecond lasers exhibit extremely large peak power values, which can be used to induce nonlinear effects (e.g., multiphoton absorption).[2–4] The simultaneous absorption of two or more photons (even photons with relatively low energy) can provide sufficient energy to cleave strong bonds. As a result, relatively long wavelength lasers with femtosecond pulse width values may be used to machine transparent materials and other materials that are traditionally difficult to machine. As mentioned earlier, materials that are micromachined using femtosecond lasers exhibit fewer thermal effects than those processed using longer pulse lasers. The micromachining resolution for longer pulse lasers depends on the diffraction limits of the optics that are used for focusing the laser energy. On the other hand, the laser energy for femtosecond lasers can be contained in dimensions that are smaller than the diffraction limits of the optics.[5] As a result, femtosecond lasers

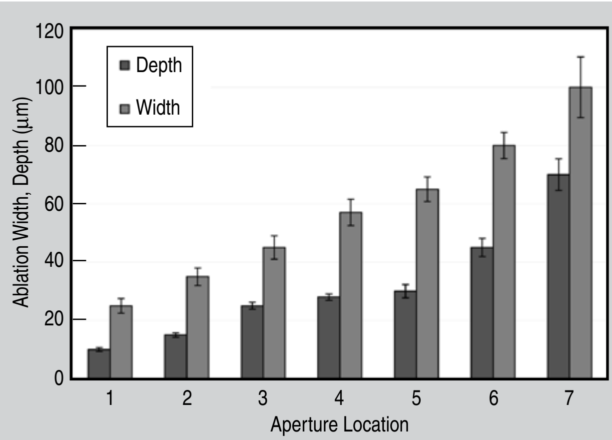

Figure 2. The relationship between dimensions of micromachined material (ablation width, ablation depth) and aperture for ArF laser micromachining of Si (111). Data is expressed as mean ± standard deviation (P<0.05).

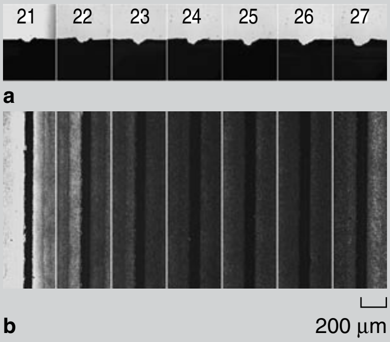

Figure 3. An optical micrograph showing ArF laser micromachining of Si (111) as a function of laser energy (shown for control voltage). (a) Cross-sectional view, (b) top-view.

enable materials to be micromachined with sub-micrometer precision.[6,7]

One attribute of laser micromachining is that small-scale features can readily be produced on a wide variety of ceramic, metallic, and polymeric substrate materials. There is negligible heat transfer beyond the region of interest on the substrate when lasers with short pulse durations are used for micromachining. Another attribute to laser micromachining is that the substrate material to be removed is vaporized and melt formation is minimized. In spite of these advantages, it should be noted that the laser micromachining may be associated with undesirable effects on the substrate material. For example, structural changes and/or stresses may be induced by laser micromachining. For example, Amer et al. have examined the microstructure of Si (111) substrates that were micromachined using a KrF laser.[8] They used Raman spectroscopy to demonstrate that laser micromachining induced tensile stress of 0.8–1.0 GPa. In addition, they reported that laser micromachining process resulted in the formation of ~14% amorphous silicon in the laser micromachined region. Amer et al. also examined the effects of laser fluence and laser pulse duration on single crystalline silicon.[9] They obtained maximum stresses for nanosecond and femtosecond lasers of 2.0 GPa and 1.5 GPa, respectively. It is interesting to note that femtosecond lasers induced significant stress and amorphization in silicon. Stresses in femtosecond laser-machined materials were attributed to laser induced shock and stresses in nanosecond laser-machined materials were attributed to thermal interactions. Their work also indicated that the induced stress was dependent on the laser fluence; peak stress values were obtained at laser fluencies of 25 J cm^{-2} and 50 J cm^{-2} for femtosecond lasers and nanosecond lasers, respectively.

BIOMEDICAL APPLICATIONS

There have been many recent advances in the development of microstructured biomedical devices for use in minimally invasive surgery and other advanced surgical techniques.[10–14] The complexity and small feature sizes required in these devices necessitates the use of laser micromachining and other advanced micromachining techniques. For example, coronary stents are medical devices that are implanted within the coronary arteries in order to maintain the flow of blood to the muscle tissues in the walls of the heart. These devices are used in conjunction with balloon catheters in order to treat lesions (blockages) in the coronary arteries.[11,15,16] Laser machining is commonly used to fabricate stents, which are hollow tubes with mesh-like walls, using stainless steel, nickel titanium (NiTi) shape memory alloy, titanium alloys, or biodegradable polymers.[1,16] Laser machining is well placed to meet the demands of an increasing number of structures on stents.[15] The use of short pulse (~0.1 ms) Nd:YAG lasers for stent fabrication may lead to the formation of a heat-affected zone, burrs, and spatter adherence as a result of heat effects. Embrittlement of metal in the heat-affected zone may lead to crack formation and expansion of the stent may lead to crack propagation and device failure. Post processing steps, including soft etching techniques involving $FeCl_3$-based solutions or pickling techniques involving dilute HCl solutions, may be used in order to achieve the required finish. Laser micromachining with femtosecond lasers can minimize these undesirable features and reduce stent processing costs.[1] Excimer lasers are widely used for micromachining of holes in catheters and patient monitoring probes. For example, probes used for analysis of pH, partial pressure of carbon dioxide, and partial pressure of oxygen in arterial blood are commonly prepared using laser micromachining. Spirals with up to five ~50 µm × 15 µm rectangular holes are micromachined onto 100 µm diameter acrylic (PMMA) optical fiber arterial blood gas probes using an ArF excimer laser. Lasers may be used to create porous probes with minimal roughness, burrs, or heat damage; these porous structures retain sufficient rigidity to be inserted within arteries.[17]

Micro-electro-mechanical systems (MEMS) have numerous potential applications, including use in implantable pressure sensors and drug delivery systems. For example, Kaihara et al.[18] used standard photolithography processes in order to create trench patterns that were similar to the branched structure of vascular networks. These templates were subsequently used for culturing patterned single-cell monolayers of liver cells. Although conventional lithography-based methods are more suitable for production of large numbers of MEMS devices, laser micromachining may be used to develop MEMS prototypes as well as patient-specific MEMS devices.

Laser micromachining may also be

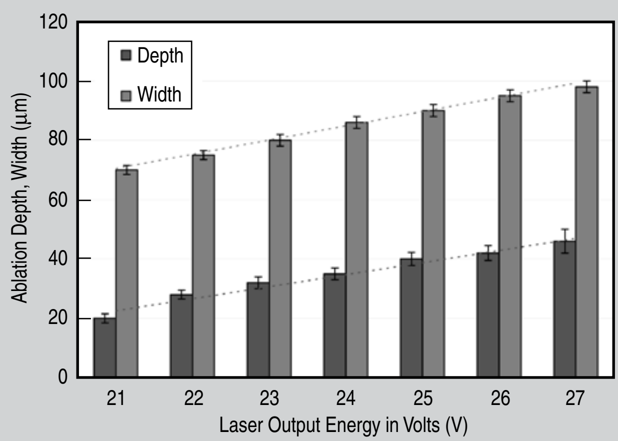

Figure 4. The relationship between dimensions of micromachined material (ablation width, ablation depth) and laser energy for ArF laser micromachining of Si (111). Data is expressed as mean ± standard deviation (P<0.05).

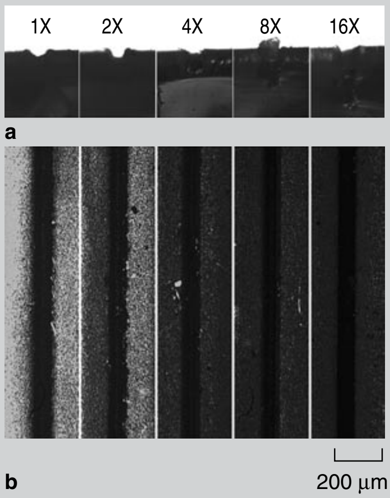

Figure 5. An optical micrograph showing ArF laser micromachining of Si (111) as a function of pattern repetition or overlap. (a) Cross-sectional view, (b) top-view.

used to create textured surfaces that support cell adhesion. For example, Soboyejo et al. used laser micromachining to fabricate microscale groove patterns on titanium-coated silicon substrates, in which the spacing between the grooves was 20 μm, the width of the grooves was ~10 μm, and the depth of the grooves was ~10 μm.[19] These patterns were fabricated using a diode-pumped solid state Q-switched laser, which provided an emission wavelength of 355 nm and a pulse width of 15 ns. They found that the orientation of cells was enhanced on surfaces with microscale grooves compared to smooth surfaces. In addition, the microscale groove patterns were shown to promote contact guidance of cells. This work suggests that structures fabricated using laser micromachining may be used to enhance implant integration with silicon-based MEMS systems.

Ti-6Al-4V is an alpha-beta titanium alloy that is extensively used in hip prostheses, knee prostheses, dental implants, and other medical devices. Surface roughening, porous coatings, and bioactive ceramic (e.g., hydroxyapatite) coatings are commonly used to enable the growth of bone-forming cells (osteoblasts) on the surface of Ti-6Al-4V implants. These modified surfaces are used to promote implant fixation by means of bony tissue growth around an implant, which is referred to as osseointegration. Conventional surface modification techniques may result in alteration of implant surface chemistry or formation of debris that could participate in implant wear. Fasai et al. used laser micromachining to produce microscale grooves for cell growth and alignment on Ti-6Al-4V surfaces.[20] Microscale grooves fabricated using ultraviolet excimer lasers demonstrated large heat-affected zones. The large heat-affected zones were attributed to the high photon energy, high-energy output top-hat laser beam intensity profile of ultraviolet excimer lasers. Fasai et al. demonstrated that diode pumped solid-state lasers were able to fabricate microscale grooves with reduced heat-affected zones.[20] ~11 μm depth and ~14 μm width microscale grooves were produced; these dimensions are considered optimal to promote cell adhesion and cell alignment.

Microfluidics is an emerging technology that involves manipulation of small volumes of fluids. Microfluidic devices have numerous medical applications, including use in clinical pathology (e.g., DNA microarrays) and clinical medicine (e.g., drug delivery devices). Many microfluidic devices contain a network of microscale channels that enable very small volumes of fluids to be assayed or tranported. Silicon and glass are commonly used to fabricate microfluidic devices because these materials are compatible with photolithography, etching, and other lithography-based technologies.[21] Laser micromachining provides several advantages over conventional methods for fabrication of microfluidic devices. Laser micromachining is the preferred method for rapid prototyping of microfluidic devices since the design of a given device may be rapidly altered through modification of the CAD data file that is used to guide the laser and/or the substrate. In addition, laser micromachining for fabrication of microfluidic devices can be performed in conventional environments; specialized or dedicated fabrication environments are typically not required. Significant efforts are underway to fabricate microfluidic devices on polymeric substrates; it is anticipated that polymeric microfluidic devices could be fabricated at low cost using laser micromachining.[22] Malek et al. have reviewed the use of laser micromachining to fabricate polymeric microfluidic devices.[5,23] Femtosecond laser micromachining may be used to fabricate three-dimensional microfluidic devices. Fabrication of embedded, three-dimensional microfluidic channels has been achieved by exposure of photosensitive glass to femtosecond laser energy followed by etching with hydrofluoric acid.[24–26] Another recent trend in microfluidics involves integrating optical, electrical, or chemical sensing elements with microfluidic channels. Laser micromachining has been used to fabricate these integrated microfluidic devices. For example, Osellame et al. have demonstrated fabrication of integrated microfluidic channels, which contained optical waveguides on a fused silica substrate.[21] Both elements of this device were fabricated on a glass substrate using a femtosecond laser. The optical waveguides in this device facilitate sensing of biological molecules in fluids that are flowing through the microchannels.

CASE STUDY: LASER MICROMACHINING OF SILICON FOR CELL ALIGNMENT

As mentioned above, silicon substrates may be used to fabricate templates for tissue substitutes as well as

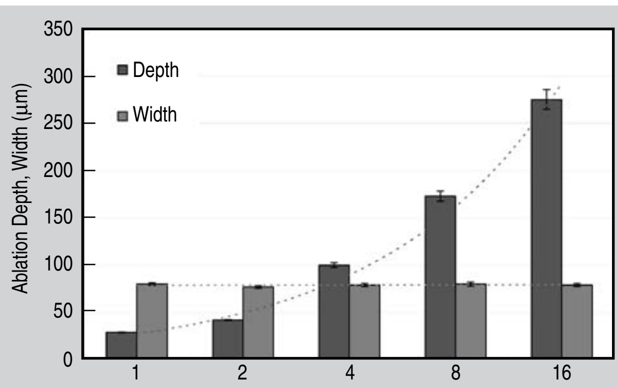

Figure 6. The relationship dimensions of micromachined material (ablation width, ablation depth) and repetition (1x, 2x, 4x, 8x, and 16x) at constant aperture size for ArF laser micromachining of Si (111). Data is expressed as mean ± standard deviation ($P<0.05$).

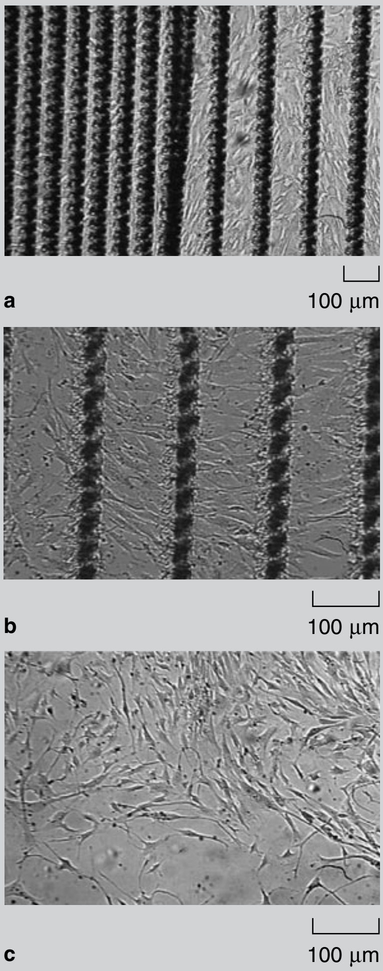

Figure 7. Human aortic–vascular smooth muscle cells on laser micromachined silicon grooves (a, b) at different magnifications and (c) on unmodified silicon surface. Images were obtained 48 hours after cell seeding.

microfluidic devices. Silicon is the most commonly used material for biomedical devices because it is inexpensive, readily available, biologically inert, and easily integrated with silicon-based electronics. In this case study, polished Si (111) wafers were used as substrate materials. A Compex 205 ArF pulsed excimer laser (Coherent, Fort Lauderdale, FL) operating at 193 nm was used to micromachine the Si (111) wafers. Two fused silica biconvex lenses were used in a telescopic arrangement to lower the primary spot size of the laser. Two apertures were used to further reduce the laser spot size and facilitate alignment. Two ultraviolet-dielectric mirrors were used to reflect the laser light at 45° incident angle. A 10× ultraviolet objective was used to focus the laser beam to spot size of up to 5 μm. A charge-coupled device camera was aligned with the mirrors and the objective in order to monitor the micromachining process. The micropositioning module was developed to convert computer-aided design file data into stage movement as well as synchronize x-y-z translation movement with laser parameters. The ablation of Si (111) wafers was examined as a function of laser energy, spot size, and repetition rate.

In one study, the aperture was varied in order to examine the relationship between laser spot size and channel dimensions. Simple line/channel patterns (with repetition of two) were developed for each aperture. The laser output energy was maintained at a constant value of 186 mJ ± 6 mJ using the voltage control setting (voltage = 25 V). Figure 1 contains optical micrographs of structures that were fabricated by laser micromachining if Si (111) wafers using several apertures (1–7). The cross-sectional image shown in Figure 1a demonstrates that an increase in aperture size was associated with an increase in the depth of ablation. The top view shown in Figure 1b indicates that an increase in aperture size resulted in an increase in the width of ablation. A higher amount of spatter was observed surrounding the channels that were fabricated using larger apertures. Figure 2 contains a graph showing the relationship between aperture size, ablation width, and ablation depth. An increasing aperture size was associated with a linear increase in depth of ablation as well as a linear increase in width of ablation.

In another study, the relationship between laser energy density and channel dimensions was evaluated. Simple line/channel patterns (with repetition of two) were developed for each laser energy density value. Figure 3 contains optical micrographs of structures that were fabricated by laser micromachining of Si (111) wafers using several energy density values, including 60 mJ (21 V), 96 mJ (22 V), 135 mJ (23 V), 162 mJ (24 V), 186 mJ (25 V), 213 mJ (26 V), and 225 mJ (27 V). The cross-sectional image shown in Figure 3a demonstrates that an increase in laser energy was associated with an increase in the depth of ablation. The top view shown in Figure 3b indicates that an increase in laser energy resulted in an increase in the width of ablation. A higher amount of spatter was noted surrounding the channels that were processed using higher laser energies. Figure 4 contains a graph showing the relationship between laser energy, ablation width, and ablation depth. An increasing laser energy was associated with a linear increase in width of ablation as well as a linear increase in depth of ablation.

Finally, the relationship between the number of repetitions (1×, 2×, 4×, 8×, 16×) and channel dimensions was examined. In this study, the aperture and the laser energy (186 mJ ± 6 mJ) were maintained at constant values. Figure 5 contains optical micrographs of structures that were fabricated by laser micromachining of Si (111) wafers using 1×, 2×, 4×, 8×, 16× repetitions. An increase in the number of repetitions was associated with an increase in the depth of ablation. The width of the channels (Figure 5b) is not significantly altered by the number of repetitions. The channel changed from a "U" shape to a "V" shape as the number of repetitions was increased (Figure 5a). The U shape is attributed to the fact that each laser spot exhibits a Gaussian spread of energy density, which in turn produces non-linear laser-material interaction. Repetitive ablation causes the central region of the laser spot to undergo a greater amount of ablation of the periphery, resulting in a non-linear transformation from the U shape to the V shape. A higher amount of spatter was observed surrounding the channels fabricated using a higher number of repetitions. Figure 6 contains a graph showing the relationship between laser energy, ablation width, and number of repetitions. There was no significant change in the width of ablation; however, the depth of ablation increased linearly with the number of repetitions.

Laser micromachining of silicon was also used to develop groove-like patterns that may be used to facilitate the orientation of human aortic vascular smooth muscle cells. Figure 7 contains optical micrographs at 48 h for human aortic vascular smooth muscle cells grown on unmodified silicon as well as on laser micromachined silicon grooves. The cells grew in non-ablated regions and formed contacts with the grooves. Figure 7b illustrates the alignment of cells between the laser micromachined grooves. Figure 7c illustrates random orientation of cells on an unmodified silicon surface. Laser micromachining may allow controlled alignment of cells as well as integration of cells with electronic devices. Spattering and other nonuniform features that may influence cell growth may be minimized through selection of appropriate micromachining parameters.

CONCLUSIONS

In this review, the use of laser micromachining for modifying medical devices and prostheses has been discussed. Several examples from the literature demonstrate that laser micromachining is a very useful technique for fabrication of a wide variety of medical devices, including stents, catheters, MEMS, and microfluidic devices. The effects of aperture size, laser energy, and repetition on ArF excimer laser ablation of silicon (111) wafers were described. In vitro studies showed that microscale grooves on silicon substrates facilitated orientation of human aortic vascular smooth muscle cells. Laser micromachining is a readily scalable process that is well-suited for modifying medical and dental devices. We anticipate that the use of nanosecond and femtosecond lasers for micromachining of stents, catheters, MEMS, microfluidic devices, and other advanced medical devices will become more significant in the next several years.

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