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Manufacturing of biomedical devices with ultrafast lasers

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Abstract

In recent years' ultra-fast lasers evolved from a device used mainly for research, to a tool for industrial material processing. Compared to other industrial laser sources, ultra-fast lasers are often linked to higher costs for additional equipment and application know how. Nevertheless, ultra-fast lasers have been used significantly in the past years for medical applications such as refractive surgery, due to their advantages compared to traditional surgery methods. Situation for manufacturing medical devices is different. Even when process developers could show better cutting quality and lower heat effect during laser cutting e.g. for benchmark applications like stent cutting ultra-fast lasers could not achieve yet a high market share for laser cutting applications. This stands in contrast with the situation for the manufacturing of medical parts. Although process developers were able to show better cutting quality and less heat effects during laser cutting, ultra-fast laser didn't manage to achieve a high market share in benchmark applications such as stent cutting, yet. The same applies for laser ablation and 3D structuring, where conventional laser technology poses a strong competition to ultra-fast lasers. This report will display new applications and approaches, which take benefit from the specific properties of ultra-fast laser pulses and show possibilities to reduce the effect of high investment costs of ultra-fast lasers on manufacturing costs. Further an opportunity for in situ process quality monitoring during 3D laser micro machining will be introduced.

Keywords: ultra short pulse lasers; ultra-fast lasers; OCT; 3D measuring

1. Surface structuring of polymers

Alongside other factors, the surface properties of a biomaterial are responsible for its acceptance by a host tissue. When tailored for improved (superior) interaction and higher attraction of favored cells, e.g. a bony or a soft tissue, an implant will integrate more successful into the host tissue. A better assimilated biomaterial is generally considered to be more successful and allows for an uneventful use according to its application. This is especially true for resorbable polymer implants. Therefore, the effect of surface structuring in different scales and the corresponding cell response to such topographically modified polymer implant materials was investigated.

This was achieved by machining the surface structures for two different cell- dimensions, with ps UV Lasers: a) sub-cellular sized features (5-20 µm) with a height of 5 µm, and

b) cell-harboring micro-wells with diameters D = 10, 30, 50 and 100 µm, depths of D/2 and spacings d = 10, 30, 50, 100 µm.

Since Laser structuring with ultra-fast pulses is a perfect tool for generating 3D micro contours in a range of 5 - 100 µm and closes the gap of process limitations between the lithography process and mechanical machining.

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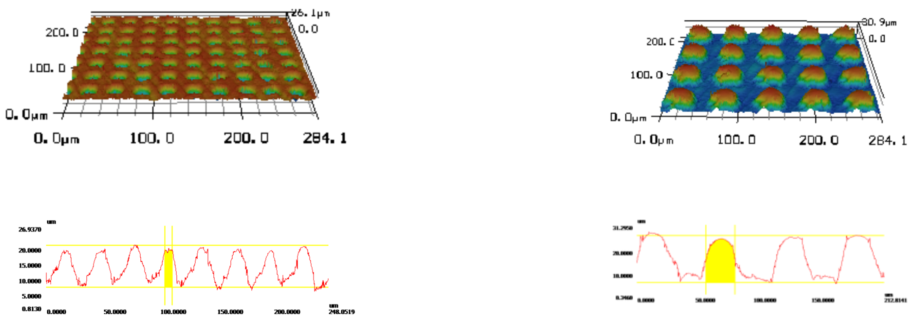


a) *b)*

Fig. 1. (a) master structure (stainless steel) generated by laser ablation (b) replication by injection molding (PLGA)

Master structures with subcellular sized features were successfully replicated into 250 µm films of PLGA by *hot* embossing and fully characterized by laser-scanning confocal microscopy (LSCM). Comparison between the topographical characterization of master and replica, respectively, revealed that high fidelity replication was achieved.

PLGA samples with a panel of different cell harboring micro-well structures were produced by injection molding. Micro-well master structures were laser machined into stainless steel and subsequently replicated into poly(phenylene sulfone) (PPSU) by hot embossing to yield inverted tone structures that served as mold inserts for *injection molding* of PLGA samples (see Fig. 2). [3]

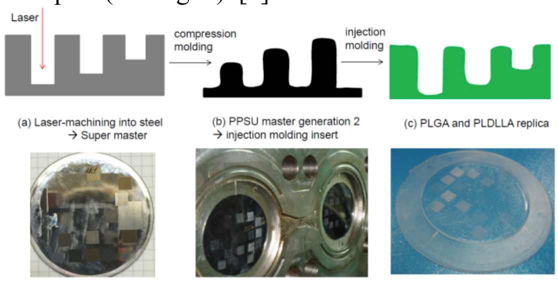


Fig. 2. Scheme of the process chain used for injection molding of PLGA substrates with a panel of different cell-harboring micro-well structures. The depicted PLGA sample (lower right) has a diameter of 6.5 cm.

2. Surface structuring of implants

One opportunity for achieving a higher biocompatibility of implants could be micro-scale surface texturing. State of the art technology for structuring are typically physiochemical processes, such as ceramic coating, electrochemical etching or micro-patterning via imprint lithography. All current methods are well suited for creating either surface topography with random feature orientation or for application on flat workpieces only. Resulting in a need for structuring technology, which enables defined micro-patterning of 3D implant surfaces. 3D laser micro-machining was investigated for structuring of stent surfaces for preventing so called restenosis, a narrowing of a blood vessel, leading to restricted blood flow. In order to achieve structures even in sub-micrometre scale a special aspherical lens setup was employed to concentrate the laser energy. This resulted in focussing diameters of about one micrometre with an elongated region of almost constant beam intensity distribution along the optical axis. Due to this type of process which uses a specific optical setup and CNC axis for machining instead of a conventional scanner, the processing time for one device is extremely long. However a cost effective manufacturing process could be achieved, by laser machining a mechanical forming die, which is able to manufacture a lot of medical devices through mechanical forming instead of direct laser machining [1].

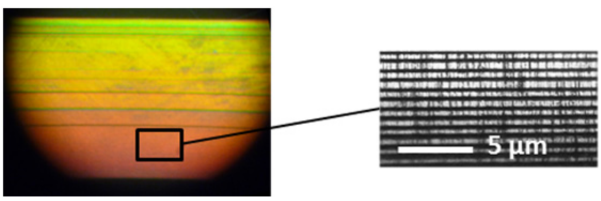


Fig. 3. Laser-ablated microgrooves in the sub-micrometre range on a curved surface acting as a diffraction grating with iridescent reflections.

To test the effect of micro-structures on endothelial wound healing, in vitro experiments were performed using a custom-made flow chamber that reproduces physiological flow conditions. It could be verified that substrates featuring a defined anisotropic topography with one micron parallel ridges (*Fig. 4*) improved the endothelial wound healing time by approx. 50 % compared to smooth, unstructured surfaces [2].

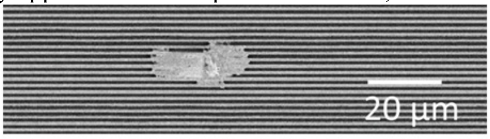
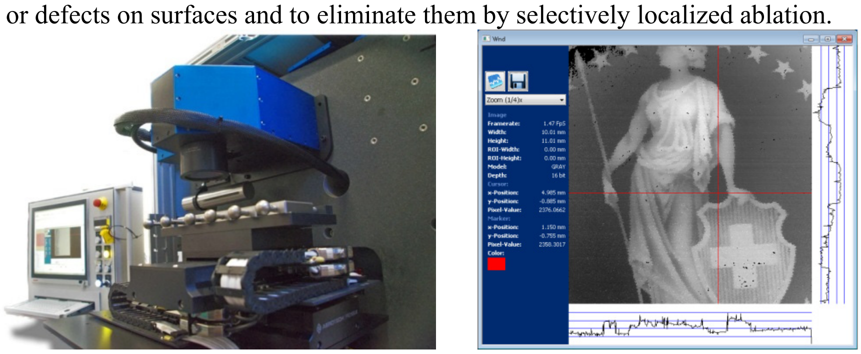


Fig. 4. Human Umbilical Vein Endothelial Cells (HUVEC) interacting with microstructured gratings: individual cell adhesion and spreading.

3. Insitu process quality monitoring during laser structuring

One challenge during 3D laser machining is the controlling and monitoring of feature dimensions, surface roughness and ablation depth. Based on a development of the WZL RWTH which demonstrated a machine integrated surface metrology system, an industrial laser processing machine was developed which integrates a Frequency Domain Optical Coherence Tomography (FD-OCT) into a conventional galvanometer scanner system. The metrology system is based on low-coherence interferometry, using a 1550 nm super luminescent diode. The depth information during the measuring is gained by analyzing the spectrum of the interferogram. The calculation of the Fourier transformation of the spectrum provides a back reflection profile as a function of the depth [4]. The system offers a measuring frequency of 70 kHz. The theoretical accuracy of the depth measuring is some 100 nm. The combination of galvanometer scanner and FD-OCT offers new opportunities for 3D laser machining with high reliability. Due to the high measuring speed and the large measuring/ scanning field, layer thickness and 3D structure size can be measured iteratively between ablation layers. Working pieces do not have to be moved or changed between laser ablation machine and measuring device. Super position between laser working beam and measuring beam prevents measuring failures. The system even offers the chance to achieve a new quality level for surface roughness. The weak point for laser ablation even with ultra-fast lasers is the propagation of surface quality and defects, during the ablation process to the final ablated structure. The initial surface quality and roughness is one determining factor for the obtainable roughness of the laser ablated structure. Identification of roughness peaks by OCT surface scanning offers the ability to detect roughness peaks or defects on surfaces and to eliminate them by selectively localized ablation.



a) b)

Fig. 5. (a) industrial solution of combined laser galvanometer scanner and FD-OCT (b) 3D profile measuring of a coin by FD-OCT measuring.

4. Marking inside of glass structures

Medical device industry is claiming high quality standards during the entire production process and high safety standards as well. Laser marking inside transparent material has been investigated and demonstrated since availability of short pulse lasers [5, 6]. Availability of galvanometer scanner coupled OCT systems expands also the opportunities of marking inside transparent materials. Ultra-fast laser marking and high speed high resolution measuring of OCT inside glass in several layers offer the opportunity to generate markers which contain information about the content of glass containers which transport medicaments or other medical relevant liquids. This method could also be used to generate secret information in any transparent material for other applications. Examples have been demonstrated.

5. Conclusion

Ultra-fast lasers have the potential to become an efficient tool for medical device manufacturing, by offering new approaches for production and allowing new product features. Especially 3D machining of production tools is cost efficient, because the high investment and manufacturing costs do not have a large impact on the product cost, in case of serial or mass production. Combination of ultra-fast lasers with FD-OCT measuring improves the manufacturing reliability and quality of 3D micro machining. The OCT also offers new opportunities for marking with ultra-fast lasers in transparent material.

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References

[1] J. Lungershausen, A. Stumpp, A. Ferrari et al.: Advanced laser ablation for the surface microstructuring of cardiovascular implants. (2013) European Cells and Materials, Vol. 26. Suppl. 1, 2013 (page 30) ISSN 1473-2262.

[2] D. Franco, F. Milde, M. Klingauf, F. Orsenigo, E. Dejana, D. Poulikakos. M. Cecchini, P. Koumoutsakos, A. Ferrari, V. Kurtcuoglu: Accelerated endothelial wound healing on microstructured substrates under flow (2013) *Biomaterials* 34(5), 1488-1497.

[3] J. Koeser, P. M. Kristiansen, R. Holtz et al. Improving resorbable polymer implants by topographical surface structuring, part II: cellular response. SNI Annual Report 2015 – Supplement, S. 82 – 83.

[4] R. Schmitt, G. Mallmann and P. Peterka, "Development of a FD-OCT for the inline process metrology in laser structuring systems", Proc. SPIE 8082, 808228 (2011)

[5] C. B. Schaffer, „Interaction of Femtosecond Laser Pulses with Transparent Materials," Harvard University, Cambridge, 2001.

[6] I. Miyamoto, K. Cvecek und M. Schmidt, „Evaluation of nonlinear absorptivity in internal modification of bulk glass by ultrashort laser pulses," OSA, 2011.