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Design, manufacture and geometric verification of rapid prototyped microfluidic encapsulations by computed tomography

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ABSTRACT

This paper presents the dimensional verification of encapsulations used to package microfluidic devices manufactured using a 3D printer of photopolymerisable resin. This characterisation has been performed by computed tomography (CT) by comparing newly manufactured encapsulations and samples that have been subjected to test conditions. Thus, it has been possible to draw conclusions both on the deviations of the nominal geometry of the encapsulations and on how this might affect their performance. This paper presents a scheme of dimensional verification from the point clouds obtained by CT. Finally, a combined threshold and scale factor correction technique of the tomography images is shown. This method is based on the simultaneous measurement of objective and master parts with known geometry. The results reveal the improvements achievable in the accuracy, given a particular machine configuration. The conclusions facilitate the improvement of the geometric design of these devices regarding their behaviour under test conditions.

1. Introduction

Additive manufacturing technologies, which are also known as layered manufacturing technologies or generically, as rapid prototyping (RP) technologies, are currently fully implemented in very different applications. Since its first industrial presence in 1988, more than 40 layered manufacturing technologies have been developed for the market [1]. These technologies effectively cover applications related to the production of prototypes in the development cycle of new products, obtaining various types of prototypes in each phase of the cycle according to the requirements of the designer or client. The latest developments on materials for prototyping, combined with appropriate post-processing techniques allow parts to be obtained in certain applications for end use. Generally, these are products for short series production, custom products or products of complex geometry, which cannot be manufactured otherwise than by layered manufacturing. RP technologies group any technology that allows a physical model to be obtained automatically from CAD data by additive layer manufacturing.

From an industrial point of view, obtaining a final piece by using additive manufacturing technologies is known as Rapid Manufacturing. Although these techniques were intended originally for purely industrial applications, at present, owing to the flexibility in obtaining complex shapes and free surfaces, one of the most widespread applications of additive fabrication is related to medical applications. In combination with imaging techniques, such as computed tomography (CT) or magnetic resonance imaging (MRI) for geometry capture and obtaining the stereo lithography (STL) format files, RP can be used in the manufacture of biomodels for surgical planning [2–4], or in surgical guides [5] for a specific patient and a specific clinical case. The use of RP also extends to applications in the field of cell biology and tissue engineering, as in the manufacture of scaffolds for tissue growth [6]. Within the field of clinical tests using microfluidic systems, it is common to use microchips for cell deposition obtained by photolithography integrated in packages that provide the fluidic connections necessary for the transport of substances into cells. The development of new tools for cell culture, based on microtechnologies, allows not only the control of the mechanical, chemical and electrical environment of biological samples but also the monitoring of their reactions in a way previously unachievable. In this way, it is possible to generate new methods for the realisation of "in vitro" tests in similar conditions as "in vivo". This

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advance is expected to promote a reduction in animal experimentation and the development of new drugs through high-throughput tests.

State-of-the-art microfluidic devices for cell culture are based on soft-lithography with the use of materials such as PDMS for the microchip manufacturing. Such devices have permitted the realisation of the first cell culture experiments on chips, proving the excellent future prospects of this technology. However, in order to achieve the full potential in biotechnological applications, a step forward is required towards reliability, handling and design flexibility of the microfluidic chips. Technology based on the polymeric material SU-8 for the chip has been developed previously and tested for clinical diagnosis applications [7,8], making possible not only the construction of microchannels but also the possibility of sensor integration and the creation of tridimensional channel platforms, among other interesting characteristics. In [9], an RP manufacturing system for tridimensional microchannels is presented, together with its later integration in a chip compatible with infrared spectroscopic imaging systems analysis. In the case of chip packaging, the geometric complexity of the connections and microfluidic channels, together with the need for integration of sensors or control and detection systems, makes this type of encapsulation difficult and costly to manufacture by conventional manufacturing technologies. It requires the use of different parts and later assembly with sealed elements to ensure adequate fluidic isolation. Often, owing to the space or geometry requirements of the channels, these parts cannot be obtained by conventional manufacturing. RP systems with smaller layer thicknesses are able to manufacture these geometries successfully; thus, it is a manufacturing technology suitable for this type of application because of both the accuracy achievable and of the biocompatibility of the materials. However, subsequent use of these microfluidic devices requires both sterilisation and prolonged biological tests under the conditions of cell culture temperatures and under the action of loads caused by the seals and the sealing elements of the package. Usually, technologies capable of obtaining the required geometry work with materials that have high coefficient of thermal expansion, which varies with temperature and that are orthotropic, working in plastic regime at low temperature. Thus, there are some problems related to the functionality of these parts and their deformation under temperature test conditions, which can result in permanent deformation that can influence the test development or the final product. Through understanding the behaviour of the materials at these temperatures and during the end use of the parts in the test, it is possible to optimise the geometry of these devices to be functionally effective and to overcome their mechanical limitations.

Verification of small parts with complex internal geometry is not possible, or is partially possible, by the use of traditional contact or non-contact measurement instruments. Therefore, the use of coordinate measuring machines (CMMs), articulated arm CMMs, and laser triangulation sensor or optical CMMs, is limited to external geometry in this type of application in non-destructive inspection. CT metrology using X-rays [10] is suitable for capturing the geometry and subsequent verification of these parts owing to the ability of obtaining both external and internal geometry via a non-contact measurement. The measurement result is a cloud of points that allows direct or indirect geometric analysis, after obtaining an STL file, by post-processing and a best-fit approach to the geometric primitives considered. Regarding the result, CT metrology is therefore a measurement technique similar to the digitalisation technologies used in quality control against CAD or reverse engineering with the addition that it also allows internal geometry to be obtained. Owing to the spread of CT in industrial dimensional metrology applications, numerous studies have been performed to model the error sources and to develop effective calibration techniques for this type of equipment [11]. Many error sources affect measurement uncertainty, which are related mainly to the CT X-ray emitter, the rotation of the workpiece during capture, the sensor that captures the attenuation in the power of the rays after passing through the piece, or the actual mathematical algorithms for reconstruction. From the standpoint of the end result, for a machine and specific measuring conditions, edge detection based on thresholding is a major influence on the accuracy of the surface reconstruction of the measured part. Furthermore, the voxel size adjustment in the reconstruction has a global influence as a scale factor in the STL obtained. Thus, edge detection and voxel size calibration and rescaling are important aspects determining the final accuracy obtained in the 2D images and the 3D reconstruction phase, such that various methods have been developed to obtain the optimum values in both cases for an accurate reconstruction of the measured geometry. For thresholding, the techniques employed to obtain values that allow an accurate separation between the material and air, or between different materials, are based on various principles, the most common being the average value of grey level between the air and material, local adaptive thresholding of grey level, maximum grey value derivatives and interpolation between voxel grey values. A good review of the characteristics and limitations of these techniques can be found in [12] and a comparison of different segmentation algorithms used in CT measurements is presented in [13]. Regarding voxel size adjustment by scaling factor, the usual method to determine the factor or factors, depending on the technique used, is to measure by CT a calibrated object together with the test part, or to measure in a CMM some geometrical characteristics of the test part following measurement by CT [10,14].

In this paper, the geometric verification and dimensional characterisation of encapsulations for microfluidic applications manufactured in photopolymerisable resin by RP in a 3D printer is presented. This characterisation is done through a new measurement procedure based on CT and on the measurement of master pieces of the same material of known geometry. This technique allows dimensional corrections based on scale factors and threshold selection to be used during the reconstructing process of the 3D geometry obtained by CT analysis. It also allows the evaluation of the accuracy obtained and improves the accuracy of the STL model, ultimately generated following the corrections. By using this technique, it is possible to verify the dimensional accuracy of the manufactured microfluidic encapsulations and to analyse the deformation suffered by the encapsulation due to test conditions, in order to optimise its geometric design.

2. Experimental methodology and setup

In this paper, four microfluidic chip packaging tools manufactured in a 3D printer (Objet Eden 350V) and two master pieces obtained by the same technique in the same material (photopolymerisable resin FullCure 720) are considered for the dimensional verification technique presented. The first step in the workflow is the 3D CAD modelling of the package and once preprocessed, it is manufactured by model and support material deposition layer by layer. The main head moves in a plane (*X*-, *Y*-axes) with movements along the *X*-axis and movements in the *Y*-direction between passes of the print head for the same layer, if it is necessary depending on the width of the workpiece. The material is released by successive head passes with a mean nominal layer thickness of 16 μm on a tray, which descends between passes (*Z*-axis), resulting in a ZFXY kinematic structure [15]. The smallest nominal dimensions to verify in the manufactured parts are the microfluidic channels that connect the lateral fluidic entry points