euspen's 18th International Conference & Exhibition, Venice, IT, June 2018
www.euspen.eu

Micro-sampling of porous media for capillary flow microfluidics

Shashwat Kushwaha[1], Benjamin Gorissen[1], Dominiek Reynaerts[1]

[1]*Department of Mechanical Engineering,*
University of Leuven
Member Flanders Make

Shashwat.kushwaha@kuleuven.be

Abstract
Rapid diagnostic testing at the site of a patient, so-called 'point-of-care' (POC) testing, is essential to provide healthcare when a fully equipped laboratory is not accessible. In developing countries, suitable POC diagnostics could yearly save millions of lives by early diagnosis of a small number of treatable conditions identified by the World Health Organization (WHO). One such POC device is being developed in KU Leuven. These devices rely on the capillary flow through 3D microfluidic channels made in porous media, which are 3D printed (3DPed). The porosity of the printed media is exploited to guide the flow through the device with embedded functional zones where remaining 3DPed regions of the device are un-wetted and form a rigid support. In order to develop a quality control process of the manufacturing, a process chain is being developed, where collecting micro-samples from the manufactured device forms an essential part. This study focuses on the destructive extraction of the samples using CNC micromilling. These samples are collected by employing layer-by-layer deconstruction of the devices leaving the zone around the point of interest available for extraction and further analysis. Required tooling, milling parameter and in process monitoring of the milling are also discussed.

Keywords: biomedical, micromachining, microsampling, microfluidics

1. Introduction

Currently available diagnostic methods fall broadly in two categories: lateral flow test and amplification based analysis. Lateral flow tests, like the home pregnancy test kit, are more suitable for the point-of-care diagnostics due to their portability and low cost. These are easy to use passive devices, do not require any external readout or electronics. In these tests, the liquid sample wicks through a porous paper-like membrane driven by capillarity and readout occurs by eye (e.g. the appearance of coloured lines). Regardless of their success, lateral flow tests are typically not quantitative, often the results are binary (positive or negative), moreover their sensitivity is limited as chemical signal amplification is not possible.

Sparked by the success of lateral flow strips, there have been many attempts to automate a timed assay sequence in so-called 'passive microfluidics' that are driven solely by capillary flow. These approaches are based on predefining 3D flow paths within stacks of porous membranes that are individually functionalized with hydrophobic/hydrophilic patterns and assay reagents [1– 4]. One such passive device is under development at KU Leuven. The proposed method employs additive manufacturing of monolithic passive microfluidic device. The devices are made by selectively sintering PMMA powder with average particle size of 50 µm. Sintering results in neck formation between particles and thus results in porosity.

The objective of extracting micro-samples from such 3D printed devices is to characterize the interior of the devices through an automated process. As the name suggests this is a subtractive process. The first stage in micro-sampling is layer-by-layer deconstruction of 3D printed objects, while machining away unwanted regions from the device, where only the sample of known volume is left at the required location (Figure 1). This sample then can be easily extracted for consecutive analysis. Nonetheless, the machining of porous material brings its own challenges. The size of the powder limits the smallest feature that can be extracted.

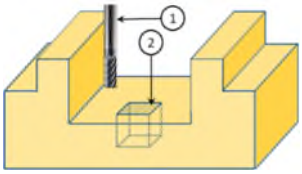

Figure 1. Layer by layer deconstruction and micro-sampling. (1): Milling tool, (2): Region of interest.

The following sections describe the machining of the 3D printed devices, while investigating temperature of machining zone and also presents the results of micro-sampling.

2. Investigation of machining temperature

The micro-sampling of the printed devices is performed on micromilling machine (KERN MMP 2522). To prepare micro-samples of sensitive components, such as antibody-labelled sections, it is necessary to verify that the temperatures during machining will not affect the bio-chemical components. Importantly, since the 3D printed diagnostics are water-activated and contain mobile assay components, dry machining is required and temperature control is essential. To qualify for safe machining, the temperature of the cutting zone must not exceed 45 °C [5].

To verify the temperature in the machining zone, a channel with a blind hole at one of the ends is cut to attach a type T thermocouple to the device using thermal grease. Another slot is then machined over the thermocouple while acquiring the real-time temperature using NI 9211, at a rate of 14 samples per second. In order to minimize the distance between the thermocouple and bottom surface of the slot, the depth of the hole is matched to the bottom of the milled slot (Figure 2).

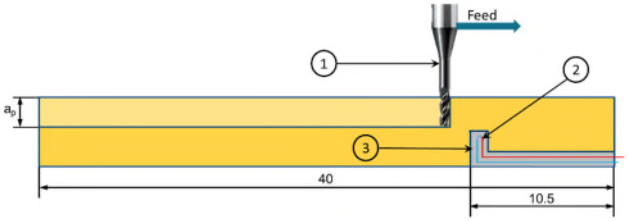

Figure 2. Thermocouple attachment and subsequent machining. (1): End mill tool, (2): Thermocouple, (3): Thermal grease.

The machining parameters to be studied are the spindle speed (S) representing cutting speed, the feed per tooth (f_z), and the depth of cut (a_p). The experiments are carried out by varying one factor at a time while keeping the other two constant. Slots of 40 mm length were milled using a diameter 1mm end mill (DIXI 7239). Table 1 lists the various machining parameters utilised for this test.

Table 1 Experiment sets for investigation of machining temperature.

Experiment set 1 S = 30000 rpm, f_z = 17 µm	Experiment set 2 S = 30000 rpm, a_p = 2 mm	Experiment set 3 f_z = 17 µm, a_p = 2 mm
a_p [mm]	f_z [µm]	S [rpm]
0.1	2	10000
0.3	3	15000
0.5	7	20000
0.7	10	25000
0.9	13	30000
1.1	17	35000
1.3	20	40000
1.5	23	
1.7	27	

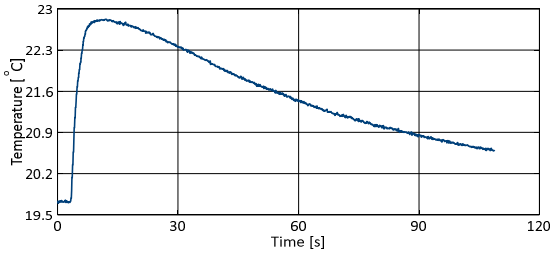

Figure 3. Temperature change measured at thermocouple, S=30000 rpm, a_p=2 mm and f_z=10 µm.

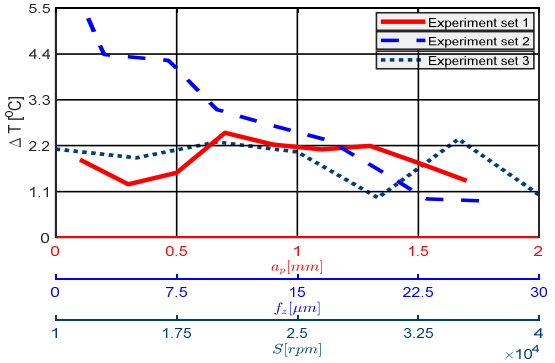

Figure 4. Change in temperature for the experiment sets.

Every experiment set is performed twice with an initial temperature between 19.5 °C and 20 °C. Total rise in temperature (ΔT) is defined as the difference between maximum temperature recorded over an experiment and initial temperature. For every experiment this is depicted in Figure 4, whereas a typical real time temperature profile is shown in Figure 3. From the performed experiments it is found that the maximum rise in temperature is not more than 6 °C for the given range of machining parameters, and it can be safely assumed the maximum temperature will remain less than 45 °C.

3. Micro-sampling

The microfluidic channels on the device are expected to have a cross section in 1 mm x 1 mm range, hence samples of 1 mm^3 are machined. In Figure 5, a digital microscope image (Keyence VHX 6000) of the machined pillars is shown. The circular pillars have a diameter of 1 mm and square pillar have edge length of 1 mm, and height of each pillar is expected to be 1 mm. Pillars are machined using diameter 1 mm end mill (DIXI 7239), and finishing passes for the machined text is performed by using diameter 0.25 mm end mill (DIXI 7240). The microscope image also reveals that the machining has only dislodged the spherical PMMA particles and the tool did not cut through individual PMMA spheres. Two such devices were machined and the dimensions of machined pillars are measured using VideoCheck FB, Werth Messtechnik GmbH, Germany and the results are enumerated in Table 2.

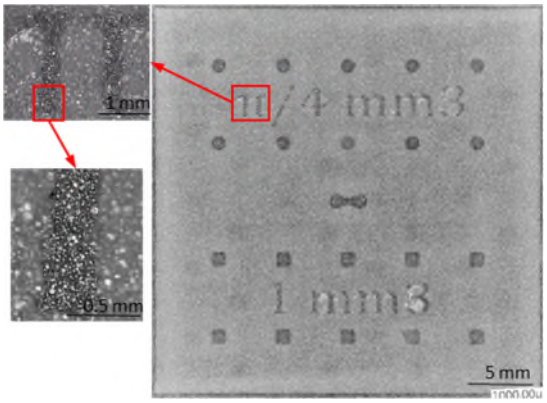

Figure 5. Machined device with pillars of 1 mm height, machined text is 200 µm high.

Table 2 Measurement results of meachined features

	Expected dimension	Mean	Standard deviation
Diameter [mm]	1	0.985	0.011
Edge length [mm]	1	0.995	0.011
Pillar height [mm]	1	1.021	0.016

4. Conclusion

A porous PMMA 3D printed microfluidic device has been investigated for feasibility of micro machining. Effect of machining parameters on temperature of the machining zone has been investigated, showing a maximum temperature increase of 6°C, which is safe for the envisioned application. Further, Micro features are machined on the device and subsequent metrology establishes the accuracy of machining, to be 11-16 µm.

References

[1] Lutz B, Liang T, Fu E, Ramachandran S, Kauffman P and Yager P 2013 Dissolvable fluidic time delays for programming multi-step assays in instrument-free paper diagnostics *Lab on a Chip* **13** 2840-47

[2] Noh H and Phillips ST 2010 Metering the capillary-driven flow of fluids in paper-based microfluidic devices *Anal. Chem.* **82** 4181-87

[3] Lewis GG, DiTucci MJ, Baker MS and Phillips ST 2012 High throughput method for prototyping three-dimensional, paper-based microfluidic devices *Lab on a Chip* **12** 2630-33

[4] Lewis GG, DiTucci MJ and Phillips ST 2014 Quantifying analytes in paper-based microfluidic devices without using external electronic readers *Angew. Chem. Int. Ed.* **51** 12707-10

[5] Takabi B and Tai BL 2017 A review of cutting mechanics and modeling techniques for biological materials *Med. Eng. Phy.* **45** 1-14