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Low Cost Production of Disposable Microfluidics by Blister Packaging Technology

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Abstract—**Large scale production of disposable microfluidics mostly is accomplished by injection moulding techniques today. A cost effective alternative to injection moulding might be vacuum thermoforming of polymer films. Vacuum thermoforming is the basis for medical and pharmaceutical packaging such as pharmaceutical blister packs. It allows for cheap and reliable forming of polymer films and thus seems suitable for the fabrication of disposables.**

Our goal is to investigate and demonstrate the potential of vacuum thermoforming for the fabrication of microtechnology components. For this purpose we have developed a simple low cost process allowing for the fabrication of disposable microfluidics by vacuum thermoforming.

I. Introduction

There is an increasing demand for disposable microfluidic devices particularly in life sciences. Applications and markets are to be found in medicine (diagnostics and therapeutics), food industry, environmental testing (e.g. field tests) and biotechnology. Applications of interest in the medical sector are Lab-on-a-Chip-Systems for Point of Care Testing [1] such as disposable blood separation microfluidics [2] or disposable nozzle structures for liquid and dry powder drugs in therapeutics. The use of disposables requires low cost fabrication and easy application of such microfluidics.

Today, high volume production of polymer based microfluidics mostly is accomplished by injection moulding techniques. Injection moulding requires a complex and expensive tooling but is very suitable for the fabrication of complex 3D-parts. However, disposable microfluidics require a predominant plane 2,5D-design. Thus, direct processing of polymer films for the fabrication of microfluidics seems promising.

At the same time low cost high volume production of pharmaceutical blister packs is accomplished by vacuum thermoforming processes. Vacuum thermoforming allows for direct large-area moulding of polymer films and thus seems suitable for the fabrication of the predominant 2,5D-designs for microfluidics.

Compared to injection moulding and hot embossing techniques the tooling for vacuum thermoforming is much easier. In particular, this becomes apparent when forming macro structures like reservoirs (see fig. 1 and fig. 5) because only one side of the tool has to be structured and the counterpart in the forming process is given by overpressure. For this reason proposed technology is promising for Rapid-Prototyping purposes as well as it seems promising for later high volume production comparable to the fabrication of pharmaceutical blister packs.

Thus, our goal is to investigate and demonstrate the potential of vacuum thermoforming for the fabrication of microtechnology devices. We develop the new replication technology using microfluidic structures exemplary as potential applications to focus on.

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II. Methods and Materials

A. Description of the tool and the process

For investigating and demonstrating purposes we have developed a heatable tool consisting of two half shells (fig. 1). The tool with the half shells and the process are based on trapped sheet thermoforming [3]. Both shells can be pressurized with vacuum and overpressure individually. The polymer film that is to be moulded seals and separates the half shells. The mould insert is located in the lower shell. In contrast to [4] we use a positive working thermoforming process so that the elevated structures of the insert define the reservoirs and fluid channels of the replica. This ensures high contour accuracy of the thermoformed microstructures. To achieve high flexibility of the tool the mould inserts can be exchanged easily. Current inserts are 15 x 15 mm^2 in size.

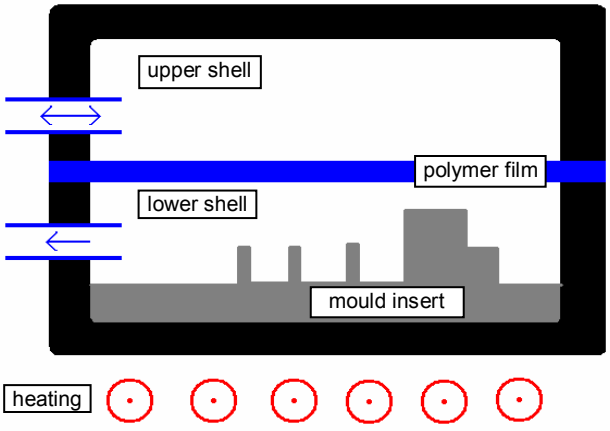

Fig. 1. Schematic of the developed tool for the thermoforming process. The heatable tooling consists of two half shells that can be pressurized individually. The polymer film that is to be moulded separates the shells.

For processing first both shells are evacuated and the

separating polymer sheet is heated above glass transition temperature. Second, the upper shell is pressurized with overpressure for moulding the polymer film while the lower shell still is evacuated. In consequence the heated polymer film is pressed onto the mould insert and structured. After cooling and demoulding the structured polymer film is sealed by a subsequent lamination process to realize liquid-tight microfluidic chips.

Process parameters for thermoforming strongly depend on the used materials. For the COC polymer films described in section *II B* we apply a process temperature of 140° C in combination with overpressure of 5 bar.

For investigating the quality of the replication process we have developed mould inserts featuring different structures. A first example comprises parallel microfluidic channels that exhibit a width of 20 µm and a height of 100 µm (fig. 2 – 4). This first example is suitable for investigating the contour accuracy of the process and the feasibility of replicating high aspect ratio microstructures. The mould insert has been fabricated by a UV-LIGA process and subsequent electroplating [5].

In a second example we use a mould insert comprising a microfluidic chip, called "Blister Chip" (fig. 5 - 7). The Blister Chip combines macroscopic fluid reservoirs ("blisters") and interconnecting fluidic microchannels. Thus, the second example demonstrates the combination of macro- and microstructures in a single insert. The second insert has been fabricated by conventional CNC milling in brass.

B. Materials

We apply polymer films for thermoforming and adequate aluminium films for sealing. Both film materials are standard in pharmaceutical packaging technology so material selection is comparable to blister packs.

The top sides of our chips are made of thermoformable high moisture barrier laminates [6]. The laminate consists of 3 layers, a COC (cyclo olefin copolymer) layer embedded in PP (polypropylene) on both sides. The laminate exhibits an overall thickness of 300 µm what alleviates demoulding and provides mechanical rigidity to the chips.

Sealing of the Blister Chips is realized by a suitable film laminate based on aluminium [6]. Depending on the application (e.g. necessity for optical transparency or use of corrosive fluids) the pharmaceutical aluminium films can be replaced by suitable polymeric sealing films.

III. RESULTS

A. First example – parallel fluidic microchannels

Figure 2, 3 and 4 illustrate results obtained by the mould insert featuring parallel fluidic microchannels. The SEM images show parallel microchannels replicated in COC by proposed vacuum thermoforming technology (fig. 2). The microchannels exhibit a width of 20 µm and a height of 100 µm and thus show an aspect ratio of 5. As the images point out high contour accuracy is obtained with our process. The edges are well drawn out and show minimum rounding. By measurements of cross sectional views radii of the edges of approximately 3 µm are deduced. Minimum rounding of the edges is essential for precise sealing of the microfluidic devices by the subsequent lamination process.

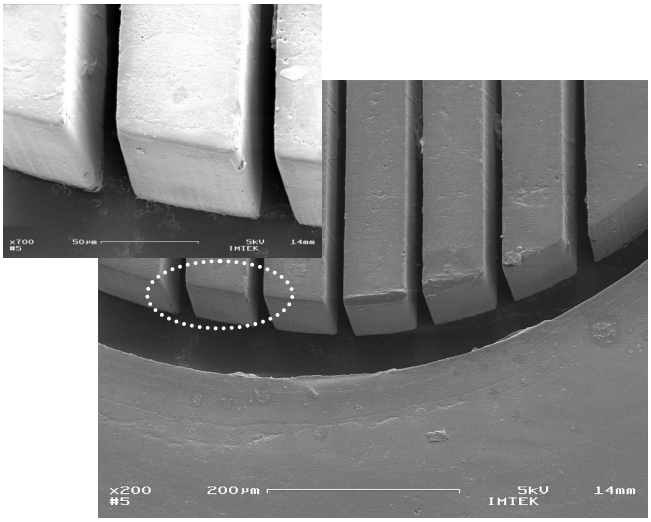

Fig 2, SEM images of parallel fluidic microchannels replicated in COC. The microchannels exhibit a width of 20 µm and a height of 100 µm. The images reveal that high contour accuracy and minimum rounding of the edges are gained by proposed process.

The micrographs of figure 3 and 4 illustrate cross sectional views of the parallel microchannel structure. The chip is fixed in cold mounting compound. To prevent small particles from accumulating in the channels we have filled up the microchannels for grinding the micrograph. The microchannels are well moulded in the PP-COC-PP laminate in which the 3 layers can be identified clearly. The aluminium film seals the thermoformed microchannels precisely and does not affect the microchannels' geometry.

As figures 3 and 4 show there are variations in layer thickness of the lower PP layer of the PP-COC-PP laminate after processing. Particularly in between the parallel microchannels this becomes apparent. The PP layer partially becomes very thin due to the high aspect ratio and the sharp edges of the microchannels. However, the PP layer predominantly is not disrupted by replicating such challenging microstructure (compare fig. 2).

Vacuum thermoforming is suitable for processing thin polymer films as the films will cover the structure compliant. However, Figure 3 proves that the novel process is capable of using thick polymer films for replication whose thickness is several times higher than the dimension of the high aspect ratio microstructure, too. Thick polymer films provide mechanical rigidity to the structured film what is favourable for demoulding after the thermoforming process. Furthermore, the thermoformed top side by itself provides mechanical rigidity to the chip. Hence, a thin aluminium or polymer film is sufficient for sealing the chip and can be applied by subsequent lamination easily.

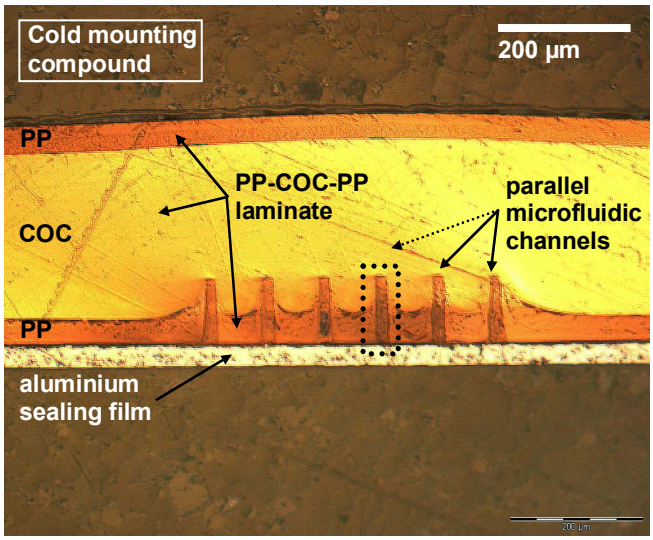

Fig 3, Micrograph, cross sectional view of parallel fluidic microchannels. The channels have been filled up before grinding the micrograph to prevent particles accumulating in the channels. The three layers of the PP-COC-PP laminate and the aluminium sealing film are visible.

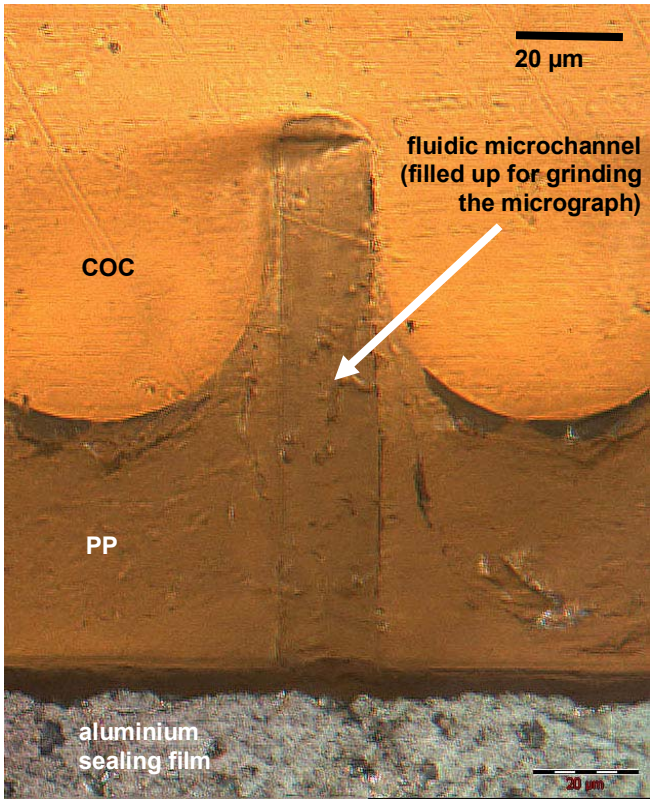

Fig 4, Micrograph, cross sectional view of fluidic microchannel from fig. 3 in detail. The channels have been filled up before grinding the micrograph to prevent particles accumulating in the channels. The microchannels exhibit a width of 20 µm and a height of 100 µm and thus show an aspect ratio of 5.

B. Second example – Microfluidic Blister Chips

The microfluidic Blister Chips have been developed as exemplary fluidic application. The Blister Chips demonstrate the feasibility of fabricating entire microfluidic devices by vacuum thermoforming and subsequent lamination. The chips combine macroscopic fluid reservoirs and interconnecting fluidic microchannels in a single insert.

Figure 5 illustrates the thermoformed top side of such Blister Chip. Fluid reservoirs (blisters) open out to interconnecting microchannels. The macroscopic reservoirs are approximately 7,5 x 5 x 2 mm^3 in size while the central microfluidic channel features a width of 1 mm and a height of 250 µm. For characterization micrographs displaying the cross section of the central fluidic channel have been generated (fig. 6). As the micrograph points out a high contour accuracy is gained. A precise sealing of the channel is accomplished and the cross section of the channel is not affected by the aluminium sealing film.

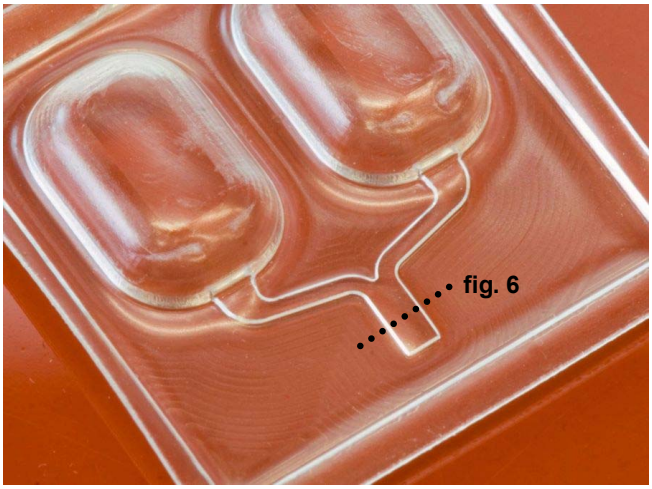

Fig. 5, Thermoformed top side of Blister Chip before laminating the aluminium sealing film. The approximate location of cross sectional view of fig. 6 is marked.

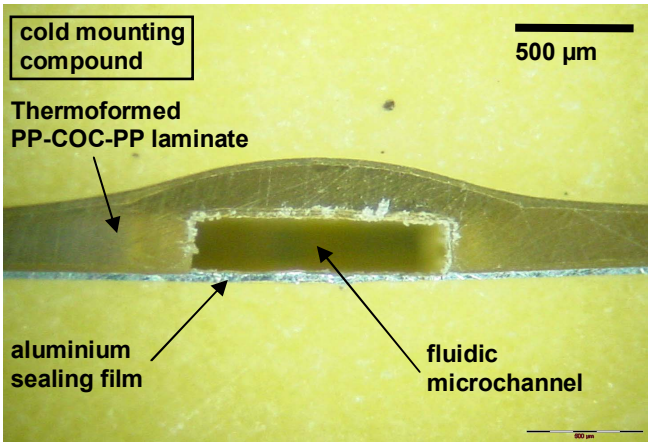

Fig. 6, Micrograph of central fluidic microchannel with aluminium sealing film. Imperfections at the channel sidewalls are due to grinding the micrograph.

Figure 7 illustrates entire Blister Chips. The translucent top side is structured by vacuum thermoforming and sealed with the aluminium sealing film by lamination. This

exemplary application of a Blister Chip can be used for storing, mixing and finally ejecting two substances that have to be stored separately before use.

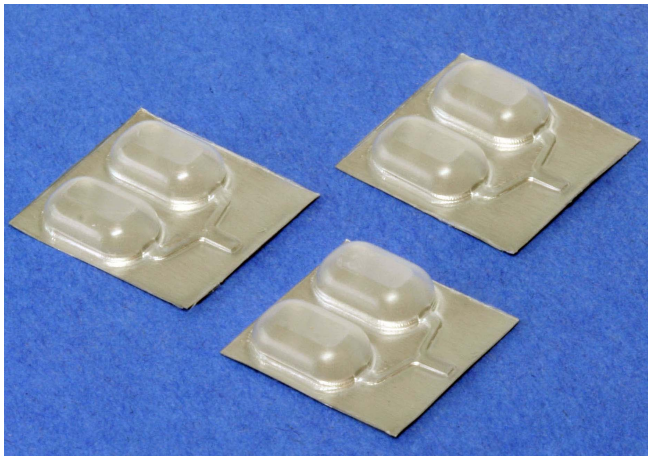

Fig. 7, "Blister Chips", thermoformed top side with aluminium sealing film. Blister Chips feature macroscopic reservoirs combined with microfluidics; chip size is 15 x 15 mm^2.

IV. Discussion

Vacuum thermoforming is the basis for medical and pharmaceutical packaging technology such as pharmaceutical blister packs. Our technology uses a modification of pharmaceutical packaging technology for the replication of microtechnology structures.

Vacuum thermoforming is capable of processing polymer films directly. The results show that particularly in combination with macro structures like fluid reservoirs vacuum thermoforming requires an easier tooling compared to injection moulding and hot embossing techniques. This is because polymer films are processed directly and there is no need for a counterpart of the tooling insert as this is given by overpressure.

Our current tool is simple and flexible what qualifies the technology for low cost Rapid Prototyping in microsystems engineering. Rapid Prototyping processes are highly suitable during design phase of microfluidics for example. Using rather a basic tool and processing we have obtained promising results. High aspect ratio microstructures as well as combined macro- and microstructures have been replicated precisely with excellent contour accuracy.

High volume production might be accomplished by parallelisation and processing large area polymer films. Processing then can be compared to low cost production of pharmaceutical blister packs and might be an alternative to injection moulding techniques at hand.

V. Conclusion

A novel technology that is suitable for low cost fabrication of microstructures such as disposable microfluidics is presented.

The flexible technology allows for the application of standard film materials e.g. of pharmaceutical packaging for the fabrication of microfluidic devices. As the results point out high aspect ratio fluidic microchannels as well as combined macroscopic and microstructures can be replicated in a single insert. Vacuum thermoforming facilitates excellent contour accuracy and thus is capable of precise fabrication of microstructures.

Due to its simple tooling and processing the developed process is highly suitable for the flexible and efficient replication of structures in microsystems engineering.

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