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Ultrasonic welding for the rapid integration of fluidic connectors into microfluidic chips

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Abstract

We introduce a variety of biocompatible fluidic connectors that can be integrated into microfluidic chips by ultrasonic welding. Commercially available barbed fittings and dispensing needles with Luer lock fittings were integrated between two chip components ensuring a fluidic in-plane contact. In addition, straight Luer lock fittings in combination with ultrasonic hot embossing, 3D printed thermoplastic connectors with Luer lock and barbed fittings were integrated out-of-plane. The integration was successful without clogging any fluidic channels.

Depending on the connector type, the pressure tightness differs. Dispensing needles showed the lowest pressure tightness of only 1.14 bar. However, all other connector types were pressure tight to at least 3.75 bar.

The main advantage of the integration technique of ultrasonic welding is the rapid implementation of individual connectors adapted to the required situation—for prototypes as well as for large-scale production. Moreover, multiple connectors can be integrated simultaneously in just one single step. This provides a user-friendly and stable connection of commonly used connector types such as barbed or Luer lock fittings for microfluidic applications.

Keywords: fluidic connector, 3D printing, microfluidic chip, ultrasonic welding, ultrasonic hot embossing

(Some figures may appear in colour only in the online journal)

1. Introduction

Microfluidic devices are required for chemical synthesis, biomedical devices, analytics, diagnostics, and for bio catalysis for pharmaceuticals and fine chemicals [1, 2]. Exemplary devices would be micro-total analysis systems or lab-on-achip systems [3–6].

Nowadays, there are enormous amounts of fluidic and microfluidic connectors [7]. In addition to plugs such as the Luer-system [8, 9] and connectors, which are supported by

magnets [10], there is a wide range of connectors that are attached by screwing Luer lock fittings or high-performance liquid chromatography fittings. These connections are mainly made of materials such as metal or thermoplastics in combination with polydimethylsiloxane (PDMS) or rubber for sealing and can be realized either out-of-plane or in-plane [7], focusing mainly on the joining method thereof. Methods such as gluing, thermal bonding, solvent bonding, laser welding and ultrasonic welding can be used to create a suitable interface [11]. Implementation of the interface with additional sealing elements such as adhesives, rubber or polydimethylsiloxane generally require more post-processing steps [7]. Laser welding requires a transparent and an absorbing joining partner or an additional absorbing layer, if full transparency

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of the whole system is required. Besides, the investment costs are high. Therefore, ultrasonic welding is a suitable and promising technique in terms of short process time, good compatibility and energy efficiency with thermoplastics. The first ultrasonic welding with microfluidic devices was reported by Truckenmüller *et al* [12]. Furthermore, the integration of microfluidic connections via ultrasonic welding by dispensing needles or polymer hoses was realized in a first approach by different groups [13–15]. However, requirements such as a low dead volume [14, 16] or the ease of plugging and removal and the compatibility with commercial tubing and fittings, reliability at higher pressures in combination with low costs, chemical inertness and biocompatibility [7, 17–20] were rarely accomplished.

In this paper, we present a variety of mechanically stable fluidic connector types, which are either commercially available or can be individually designed and produced rapidly by 3D printing or ultrasonic hot embossing [21–28]. The integration in microfluidic chips is performed by ultrasonic welding, resulting in a biocompatible and fast connection technology.

2. Material, fabrication and methods

Ultrasonic welding requires so-called energy directors (ED) on one joint partner. The ultrasonic vibrations transmitted by a horn locally plasticize the ED and generate molten material for the welding seam [29, 30]. The melting process and the melt flow can be influenced by the ED geometry. Beside this, the material combination plays an important role for successful welding and tight welding seams. Ideally, connector and chip are made of the same polymer to provide similar glass transition temperatures and molecular structures as key factors for successful welding [29]. So, both joint sides melt at the same time and at the same temperature. If the difference in the glass transition temperatures is too large, only the joining partner with the lower glass transition temperature melts and fills the cavities of the counter joining partner without a material-locking connection.

All connectors were welded on chip inlets using a 35 kHz ultrasonic welding machine PS DIALOG digital control 1000 (Herrmann Ultraschalltechnik GmbH & Co. KG, Germany). These inlets consisted of either Polycarbonate (PC) (Makrolon[®] GP clear 099, Covestro AG, Germany) or Polyethylene terephthalate (PET) (MEDIPAK AG, Switzerland). Both materials are suitable for microfluidic chips [31–35] because of their transparency, low water absorption, very good biocompatibility, high strength, stiffness, hardness, tenacity and good ultrasonic weldability [36].

Upper chip parts with ED and the lower chip parts were produced by micro milling, the chip inlets were constructed by ultrasonic hot embossing. All connectors were welded with a flat titanium horn, while both joining partners were fixed with corresponding supports. The output amplitude of the converter (6.5 μ m) was amplified to 16.1 μ m through a 1:1.5 booster and the 1:2.2 transformation of the horn. The clamping force was 120 N.



Figure 1. Schematic drawings of various connector types: (a) dispensing steel needles with different diameters; (b) straight barbed connector with two radial ED; (c) straight Luer lock by drilling out a Luer lock screw cap; (d1) 3D printed straight Luer lock; (d2) 3D printed 90° angled elbow Luer lock; and (d3) 3D printed 90° angled elbow barbed fitting.

2.1. Connector types

2.1.1. Dispensing needles. Two different dispensing needles (Nordson EFD, USA) with a Luer lock-fitting on one end and steel needles with 1.36 mm and 0.51 mm inner diameter (ID) on the other end were used (see figure 1(a)). The metal needles were sandblasted to increase surface roughness, thereby improving the adhesion between the plasticized ED and the metal. The ED was designed so that its excess melt surrounds the rough metal needle and tightens the welding zone at the PC's chip inlet (see figure 2(a)) [21]. Therefore, a square cross-section having a width of 400 μ m was selected. For better mechanical stability, the dispensing needles were integrated in-plane.

2.1.2. Straight barbed connector. Commercially available straight barbed PC connectors with 1.60 mm (1/16'') ID were selected (Value Plastics dba Nordson MEDICAL, USA). These connectors provide additional structures that serve as a radial ED in the chip inlet (see figure 1(b)). They were also welded in-plane in PC chip inlets similar to the dispensing needles (see figure 2(b)).

2.1.3. Ultrasonic hot embossed structure for commercial Luer lock connectors. In addition, ultrasound can be used to emboss structures by the support of thin foil stacks or by heating the embossing tool, which is referred to as ultrasonic hot embossing [26-28]. In this work, the fluidic inlets on the PC chip surfaces were rotationally symmetric microstructured with an ED by means of a brass embossing tool in order to create the possibility to ultrasonically weld any flat connectors out-of-plane. In contrast to the connector types of sections 2.1.1 and 2.1.2, the ED was surrounded by drains [21] to prevent clogging of the inlets by ED excess melt [14] (see figure 2(c1)). Subsequently, a commercially available female Luer lock screw cap (Cole-Parmer GmbH, Germany) (see figure 1(c)) was drilled out and its flat side welded on this structure (see figure 2(c2)). Alternatively, the connector can be microstructured analogously to the chip and welded to an unstructured chip inlet (see figures 2(d1) and (d2)).



Figure 2. Schematic cross-sections of various connector types prior to ultrasonic welding in-plane or out-of-plane. (a) Dispensing needles or (b) commercially available straight barbed connector are integrated in-plane between two chip parts. (c1) Fluidic inlets are microstructured by ultrasonic hot embossing to create ED and drainage for ultrasonic welding (c2) of any flat connector. (d1) Conversely, each flat connector can be microstructured by ultrasonic hot embossing to create ED and drainage for ultrasonic welding (d2) on a flat chip inlet. Analog to (d2), individual connectors with ED and drainage with common connector types as Luer lock and barbed fitting can be manufactured with a fused deposition molding 3D printer and welded on chip inlets.

Table 1. Finning parameters for FC and FET manie	Table 1.	e 1. Printing	parameters	for PC	and PET	filamen
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	Filament material		
Printing parameter	PC	PET	
Printing speed (mm s ⁻¹)	20	30	
Travel speed (mm s^{-1})	120	120	
Nozzle temperature (°C)	255	210	
Heat bed temperature (°C)	110	75	

2.1.4. Connectors with barbed or Luer lock fitting and integrated energy director with drainage. Individual connectors with ED and drainage analog to the connector described in 2.1.3, which have either a barbed or a female Luer lock-fitting, were manufactured by 3D printing. This method was selected for prototyping. If higher quantities are required and the feasibility is available, connectors with suitable designs can be injection molded.

To print connectors of thermoplastic material a fused deposition molding 3D printer (Ultimaker 2 +, Ultimaker B.V., The Netherlands) was used. As filaments matching to the material of the chip either PC (Polymaker, China) or PET (Innofil3D, The Netherlands) were used. The materials were



Figure 3. Schematic drawing of the experimental setup for measuring the maximum pressure of the connectors according to Perozziello *et al* [8].

3D printed using a 0.25 mm nozzle with the parameters shown in table 1.

In order to be able to couple in the ultrasonic energy, the horn must be positioned in such a way that it covers the entire area of the ED. Therefore, each connector has been designed to provide a flat surface for the horn.



Figure 4. Maximum pressure tightness of the ultrasonically welded connector types. The highest pressure tightness was achieved by the thermoplastic connectors. The combination of the two different materials metal and thermoplastic causes a lower pressure tightness. Nevertheless, a slimmer fitting of the channel in the chip and a smaller diameter of the dispensing needles resulted in a higher pressure tightness (1.14 bar) compared to the larger dispensing needles (0.58 bar). The straight barbed connector, the connector welded on ultrasonically hot embossed ED and the 3D printed connectors withstood the maximum available pressure of 3.75 bar.

While the straight Luer lock design provides a larger flat contact surface for ultrasonic welding (see figure 1(d1)), the round-shaped and 90° angled connectors require a cubic 90° angle (see figures 1(d2) and (d3)). To achieve the best print quality, the printing orientation of the connectors was chosen to be rectangular to the ED and drainage structure. Like the connectors in section 2.1.3, the 3D printed connectors were welded onto the chip making contact between the connector's flat side with horn and the chip inlet's with the ED and drainage structure (see figure 2(d2)). These connectors were welded on chip inlets of PC or PET. We also tested welding of dissimilar polymers.

2.2. Pressure tests

To test the maximum pressure that the welding seams can withstand, the connectors were welded onto chips with deadends. The different connector types were connected via a pressure reducer to compressed nitrogen, then were immersed in a water-containing beaker according to Perozziello *et al* [8]. The pressure was gradually increased to a maximum pressure of 3.75 bar, provided by the compressed nitrogen pipeline inhouse. This procedure was performed until the connection leaked or withstood the pressure for at least 1 h. For the entire test, the pressure was read out continuously by a WIKA model A-10 pressure transmitter (WIKA, Germany) and recorded with a frequency of 100 Hz on a PC via LabVIEW for a precise measuring of the pressure drop, as shown in figure 3. In case of a leakage, the maximum pressure corresponded to the recorded pressure drop.

2.3. Preparation of cross-sectional images

To validate the quality of the welding seams, cross-section cuts were made of each welded connector using a two-step process. A bench grinder (ECO, 230 V, Reichmann & Sohn GmbH, Germany) produced a 'pre'-cross-section, which was then embedded in the acrylic mounting system DuroCit-3 (Struers, Denmark). Small capillaries were separately filled prior to embedding to remove trapped air and to ensure proper filling. Subsequently, the embedded connectors were carefully and slowly ground with silicon carbide paper of different grit sizes (P400-P2500, Struers, Denmark) and the grinding and polishing machine Saphir 350E to the cross-sections (ATM GmbH, Germany). Between each grinding step, the samples were cleaned with water to remove any remaining abrasive from the previous step. This elaborate procedure was urgently required to avoid distorted cross-sections, which are often generated by mere sawing, e.g. smearing or ablation of fine structures or edges. Finally, each cross-section was sputtercoated (K575X Sputter Coater, Quorum Technologies Ltd, UK) with Au/Pd and recorded with scanning electron microscopy (SEM) (Supra 60VP, Zeiss, Germany).

3. Results and discussion

3.1. Weldability of the fluidic connectors

With optimized welding parameters, all connectors were successfully and reproducibly welded with ultrasound. An exception was the 3D printed connectors welded on a dissimilar polymer, which broke immediately after removing it from the fixture. As expected, welding the dissimilar polymers PC and PET showed poor weldability. In addition, the leverage to break is higher for connectors welded out-of-plane than in-plane.

A difference between connectors of PC or PET was not observed. Only dispensing needles showed a lower reproducibility due to the production tolerances of the dispensing needles and the micro milled channel respectively. 3D printed elbow connectors with too long appendages broke when ultrasonic welding vibrations led to too strong oscillations, this finding corresponds to Rotheiser's [29]. This effect has been enhanced by the layer-wise printing at fused deposition



Figure 5. SEM images showing cross-sections of the ultrasonically welded connectors. White dashed ellipses indicate the welding seams. Thermoplastics and metal appear smooth grey, while the acrylic mounting compound appears rough and trapped air black. The white scale bar is 500 μ m. (a) Schematic cross-section of an ultrasonically welded connector in-plane. (b) Welding seam of the dispensing needle with an ID of 1.36 mm. (c) Welding seam of the dispensing needle with an ID of 0.51 mm. (d) Welding seam of the straight barbed connector. (e) Schematic cross-section of an ultrasonically welded connector out-of-plane. (f) Welding seam of the straight Luer lock. (g) Welding seam of the 3D printed straight Luer lock connector.

molding and can be reduced or avoided in the manufacture of these connectors by injection molding. However, it was also possible for each connector type to simultaneously weld multiple connectors in one chip. The minimum distance between each connector is limited by the dimension of tubings and the male Luer lock while the welding seam itself is too small to be a restriction. It should also be taken into account that there is sufficient space for mounting/demounting of the counter connector. In case of in-plane connectors, all connectors must be welded simultaneously to avoid material tensions between welded and unwelded areas.

3.2. Pressure tightness

The maximum pressure measurements showed different pressure tightnesses depending on the connector type (see

figure 4). The dispensing needles had a low tightness and bubbles appeared immediately after the maximum pressure was exceeded. A slimmer fitting of the micro milled channel in the chip and a smaller diameter of the dispensing needles resulted in a higher pressure tightness. As for welded dispensing needles with an ID of 0.51 mm, bubbles occurred at 1.14 bar. Compared to this, the larger dispensing needles were tight to a pressure of 0.58 bar, when bubbles appeared. We assume that the smaller dispensing needles were more easily enclosed by the plasticized ED, especially since the flow paths of the melt are shorter. The general result of joining the two different materials (metal and thermoplastic) was limited tightness. In addition, the lower welding reproducibility of the dispensing needles is underlined by high standard deviations of the maximum pressure tightnesses in figure 4.

The other connectors were tight for at least 1 h at 3.75 bar showing no bubbles. The in-plane integration of the straight barbed connector allows the lowest total chip height of all connector types.

The connectors welded on ultrasonically hot embossed ED and the 3D printed connectors represent a tight, stable and highly flexible mountable connector type.

Due to the 90° rotated plane (y-z) of the 3D printed fittings during 3D printing, the 90° angled elbow Luer lock and the barbed fittings did not have a perfectly tight connection to the counterparts during the first pressure tests. Bubbles occurred at these connections to the counterparts. Therefore, these counterparts were additionally fixed and sealed with adhesive (DYMAX 1187-M, DYMAX, USA) in order to test the tightness of the welding seam itself. A difference between 3D printed connectors made of PC or PET could not be observed.

3.3. Cross-sectional images

All images of cross-sections are shown in figure 5 which demonstrate ultrasonic welding without clogging the fluidic channels. In the case of dispensing needles, the melt of the ED had to flow around the metal needle and into the pores of their sandblasted surfaces. However, on the cross-sectional image there are some small capillaries showing that the melt did not flow in each pore (see figures 5(b) and (c)). These small capillaries lead from the chip interior to the exterior and create a leakage, substantiated by the measured low pressure tightness of both dispensing needles. The welding seam of the dispensing needle with an ID of 1.36 mm shows more capillaries compared to the welding seam of the dispensing needle with an ID of 0.51 mm, resulting in a 0.56 bar higher pressure tightness. However, this connector type does not seem to be recommended for every application according to the combination of the two different materials.

The welding seam between the straight barbed connector and the chip is not visible due to a homogeneous welding of the same material (see figure 5(d)). Similarly, the straight Luer lock, which is welded to the hot embossed chip, shows a homogeneous and tight welding seam (see figure 5(f)). Both connector types show the most homogeneous welding seam.

3D printed straight Luer lock, 90°-angled elbow Luer lock and 90°-angled elbow barbed fitting show tight cross-sections. In addition, printing layers and some trapped air can be recognized, which do not affect the tightness, in contrast to the capillaries on the dispensing needles. All these connectors have been studied, but due to similar results between PC and PET, only one SEM image is shown (see figure 5(g)).

4. Conclusion

Steel dispensing needles of different diameters, straight barbed connector, straight Luer lock by drilling out a Luer lock screw cap, 3D printed connectors with Luer lock and barbed fitting were in general welded successfully and reproducibly with ultrasound, without clogging the chip inlet. Poor ultrasonic welding was generally due to excessive production tolerances of the joining partners or insufficient fixation during ultrasonic welding. Only connectors welded with dissimilar materials showed limited stability and tightness.

The tubes were connected in a user-friendly and stable way. Depending on the connector type, the connectors were resistant to different bursting pressures.

The welding zone of the dispensing needles must be a few 100 μ m too small to produce a tight welding seam. The maximum pressure tightness was thus 1.14 bar.

Due to the thermoplastic material and design of the ED, the other connector types were fully pressure tight up to an average in-house pressure of 3.75 bar. This has the advantage that a biocompatible and commonly used fluidic connector type, such as barbed or Luer lock fitting, is in an individual shape and design that can be adapted to the required situation. In addition, these connectors can be manufactured in large quantities with higher quality, stability and lower costs by injection molding.

These connectors are therefore very well suited for various types of thermoplastic and biocompatible chips for microfluidic and macrofluidic applications in chemical synthesis, biomedical devices, analytics, diagnostics and biocatalysis of pharmaceuticals and fine chemicals as well as for large-scale production in combination with ultrasonic welding.

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