PAPER MEMS CHIP FOR INK-JET PRINTER-LIKE CLINICAL AUTO ANALYZER

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ABSTRACT

New concept of paper-based devices (we call "paper MEMS chip") and ink-jet printer-like analyzer for clinical diagnostics is presented. A water-resisting paper coated with poly-olefin resin was selected for the chip's material, and the micro-channels were successfully fabricated by using hot-embossing process on the paper. Pressure resistance was evaluated by feeding water into the micro-channel of a paper chip and the channel could stand practical pressure level more than 100 kPa. Liquid flow driven by capillary force was observed in the proto-type of paper MEMS chip.

KEYWORDS: Paper, Clinical auto analyzer, Hot-embossing, Capillary

INTRODUCTION

Clinical auto analyzers for blood examination are essential equipments for medical diagnostics through their accuracy and fully automatic operation. However, their stand-alone size, not affordable price prevent them from being widely used in clinics. Micro total analysis systems (micro-TAS) will be an alternative to conventional clinical auto analyzer because they have precise structure for accurate operation and small enough. As a base material for micro-TAS, Silicon, plastics and PDMS have been mainly used because of the accuracy of form, but still have cost problem for disposable usage[1]. On the other hand, paper material has been used in clinical simple test, for instance, dry chemistry[2] and immuno-chromatography, because paper is extremely low cost material appropriate for disposable usage and suitable for burning sterilization with a little production of toxic substances. However, since the structure made of paper is lacking for accuracy of form and durability especially against liquid, there has been a lot of difficulties to apply paper to micro-TAS as the base material. Therefore, as a first step, we focused on improving the accuracy of form and durability of the paper (challenge item 1), and secondly providing fully automated function such as pumps, valves, and detectors on the paper (challenge item 2). Some solutions for these problems have already been come up with. In this paper, we describe challenge item 1, that is, forming process of micro-channel on the paper and durability against liquid.

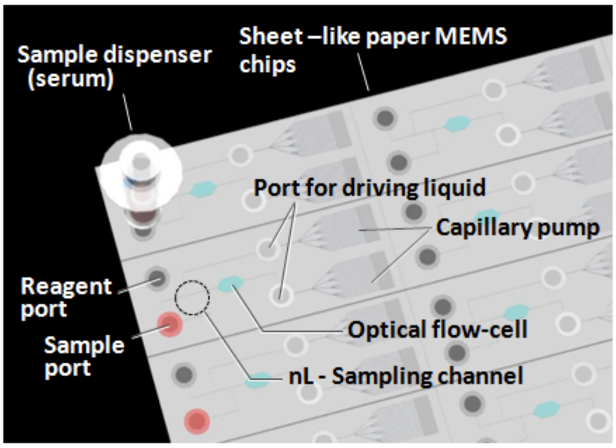

Figure 1: Sheet-like paper MEMS chips

CONCEPT OF INK-JET PRINTER-LIKE CLINICAL AUTO ANALYZER

Figure 1 shows the configuration of sheet-like paper MEMS chips. Figure 2 shows the conceptual image of a clinical auto analyzer for the disposable chips. Different kind of micro-fluid circuit corresponding to testing item are fabricated and arrayed on the paper sheet. Every function for metering sample and reagent is fabricated in the disposable chip. Therefore, the prime constituents of the analyzer are only micro-dispensers for reagent and driving liquid, and a sheet loading mechanism, which are similar to those of a ink-jet printer. As shown in figure 1, a droplet of sample is put into each sample port in the sheet by using a sample dispenser manually and the sheet is inserted into the analyzer. As shown in figure 2, the sheet is moved forward and backward with the reagent and the driving liquid being dispensed sequentially. By dispensing driving liquid, the capillary pump on the chip starts to suck the sample and the reagent into the micro-channels. The sample is metered at a nano-litter-sampling channel and mixed with the rea-

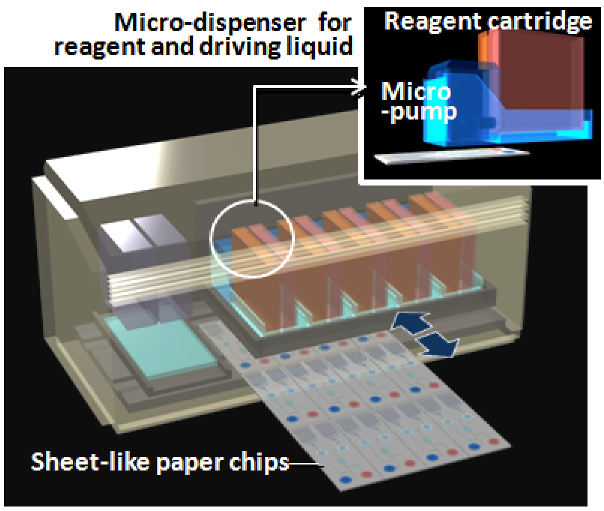

Figure 2: Concept of printer-like clinical auto analyzer

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gent. Mixed liquid is shipped to an optical flow-cell and detected optically.

FABRICATION PROCESS

Figure 3 shows the materials of the chips and a fabrication process. A paper coated with poly-olefin resin (NIPPON PAPER PAPYLIA Co., Ltd, OPER Series, total thickness: 300 µm, resin layer: 20 µm) was used as a base material because of its good water-resisting property. The coated resin has a role of water resist and bonding layer, either. Cellophane film (thickness: ~36µm) coated with poly-lactate resin and polyurethane film (thickness: ~25µm) coated with acrylate resin as a bonding layer were selected as cover films. Si-die with micro-structures is made by using dry etcher (DRIE). The depth of the structures was 30 µm.

As shown in Figure 3, first, (1) the paper surface was flattened. Then, (2) micro channels were embossed with the Si-die under the application of heat. In order to shaping the channel precisely, the embossing condition (heat temperature, pressure, and time interval), the condition of the paper (thickness, surface roughness, etc.), and a pad under the paper (material, thickness, etc.) were carefully investigated. Especially, the heat temperature kept a little lower degree (= 95 degree) than the melting temperature of the resin in order to prevent the layer from being damaged and a deformable sheet as the pad was selected to pressurize the paper uniformly. After forming the micro channels, (3) the surface of the paper and the cover film were cleaned by using ethanol. Next, (4) the cellophane film was bonded under applying heat, which temperature was 95 degree for 60 second. In the case of polyurethane film, it was bonded under room temperature.

LIQUID FLOW ON PAPER

In order to check water-resisting property, pressure test was done by using a paper chip with single channel as shown in figure 4 (upper photo). The channel width was 100 µm, depth was ~30 µm, and covered with cellophane film. Figure 5 shows the experimental setup of the pressure test. A syringe pump flowed water into the inlet of the chip and the pressure near the inlet point of the test chip was measured by using a pressure sensor (KEYENCE AP-43). If the channel is firm and not broken, the pressure keeps same value. Figure 4 (lower photo) shows the photo of water poured from the outlet of the paper chip. Figure 5 shows the measurement result of the pressure. The pressure keeps constant (around 135 kPa) for more than 30 min. Since the connecting tube between the sensor and the inlet of the test chip is 36 mm in length and 125 µm in inner diameter, the pressure loss in the micro-channel of the chip itself is calculated to be 130 kPa (the pressure loss of the connecting tube is calculated to be ~20 times as small as that of the micro-channel). This water-resisting property is feasible for micro-TAS .

To check the accuracy of form, the proto-type of a paper MEMS chip was fabricated. Figure 6 shows the schematic configuration of Si-die, and the photo of the Si-die made by using DRIE. Figure 7 shows the photo

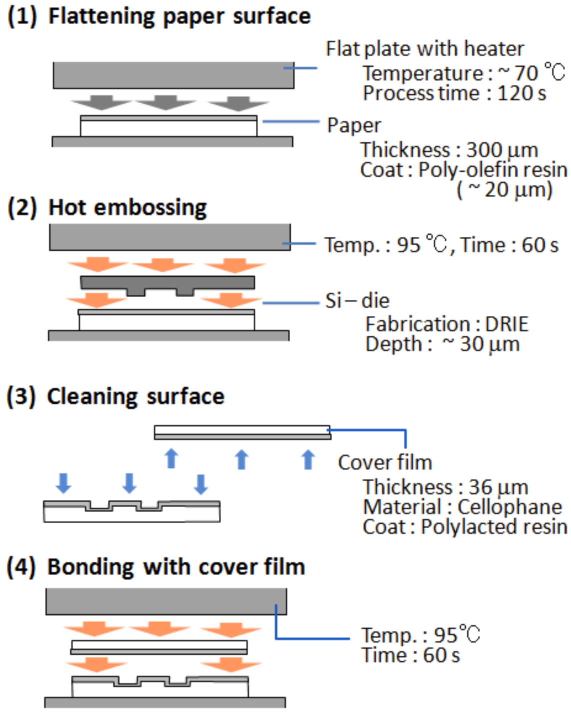

Figure 3: Materials and fabrication process

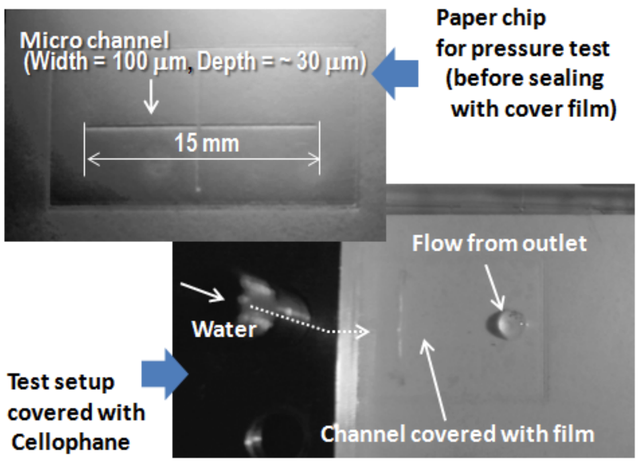

Figure 4: Paper based chip for pressure test

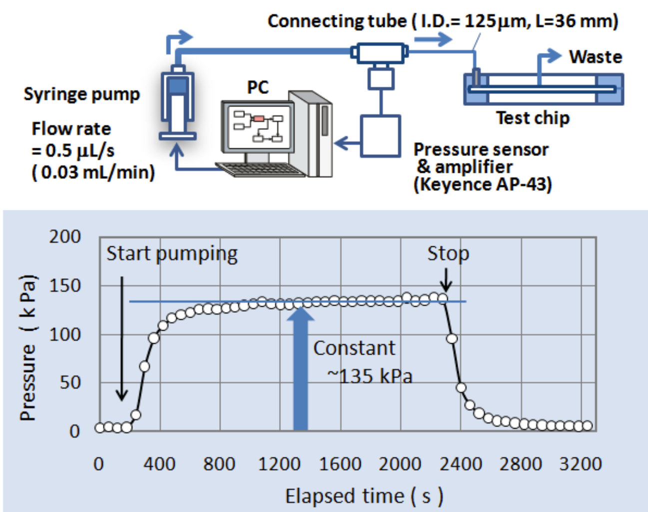

Figure 5: Experimental setup and pressure-test result

of the chip after embossing, and the enlarged view of a sampling part and a capillary pump. The micro-structures were formed precisely, and even the narrowest channel, which width was 50 μm, was formed successfully.

Figure 7 shows liquid flow at the point of capillary pump. In this case, the chip was covered with the polyurethane film. The dye (new methylene blue) was diluted with ethanol in order to increase capillary force and accelerate the flow speed. The dye was dropped at the point of the port for driving liquid. It was observed that the dye moved to the capillary pump channels smoothly. As a result, these materials and fabrication method are feasible for the disposable chip.

CONCLUSION

New concept of paper MEMS chip and ink-jet printer -like analyzer for clinical diagnostics was proposed. A water-resisting paper coated with poly-olefin resin was selected for the chip's material, and micro-channels were successfully fabricated by using hot-embossing process on the paper. Pressure resistance was evaluated by feeding water into the micro-channel and the channel could bear practical pressure level more than 100 kPa. Liquid flow driven by capillary force was observed in the proto-type of paper MEMS chip. As a first step, it was confirmed that these paper materials and fabrication method were feasible for the disposable chip.

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[2] http://www.fujifilm.com/products/medical/clinical_chemistry_system/

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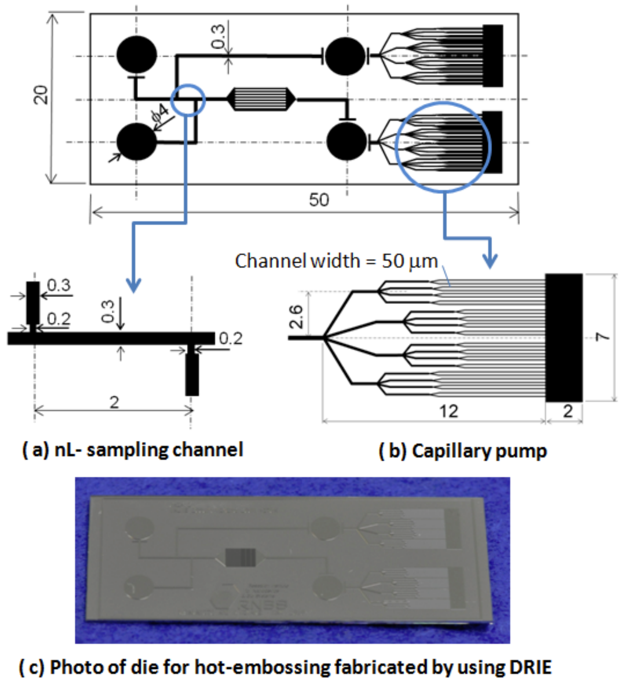

Figure 6: Configuration of die for first proto-type

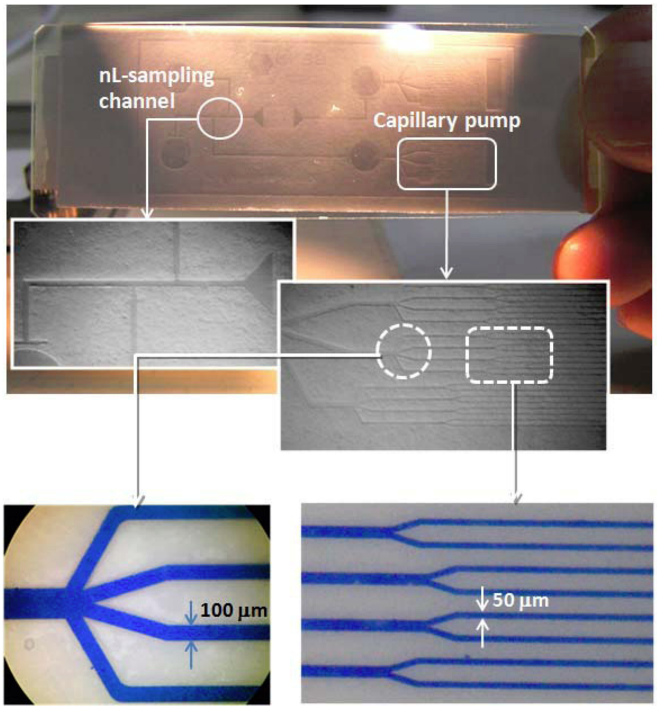

Figure 7: Photo of fabricated chip and visualization of dye driven by capillary pump