Abstract

A painless blood collection system which combines a Si needle array chip with a centrifugal separation chip using a U-shape channel has been developed aiming at the biochip checking our health at home. Two-steps etching of a Si(100) substrate employing hydrazine and then TMAH improved density of Si needles. The whole blood obtained by piercing the Si needles with a spring force into capillary vessels was conveyed to the backside of the substrate through holes dry-etched on its bottom by a vacuum power. This blood as is was introduced directly to the U-shape channel fabricated on a PET plate and separated to blood cells and plasmas by the centrifugation.

Keywords: Biochip, MEMS, Painless needle, Si tip, On-chip centrifugation

1. Introduction

A variety of biochips examining healthcare/disease by analysing trace amount of the blood have attracted much attention. A key technology for the goal is painless collection of the blood. We had already reported the painless needle fabricated by sharpening at a 10 degree a tip of a SUS tube with a diameter of 100 μm [1]. The sharpness and thinness of the needle did not make all of our researchers feel any pain. However, we sometimes failed in collection of the blood due to obscure location of the vein. To solve the problem, it will be reported in this symposium that the detection systems of the vein location utilizing both near infrared irradiation and electrochemical effects generated when the needle arrived at the vein surface. Another solution is collection of the blood from capillary vessels. So far, some works reported extracting the blood through holes fabricated on tips of sharp Si needles utilizing MEMS (micro electromechanical system) technology [2,3]. In this paper, we report a new structure in which Si needles and through-holes are separately responsible for piercing into a capillary vessel and extracting the blood, respectively. A manufacturing process of a painless Si needle array chip and a collecting method of the plasma from a PET (polyethylene terephthalate) chip performing the on-chip centrifugal separation of the blood are also described.
2. Experimental

Figure 1 shows a fabrication process of the Si needle array chip. A Si(100) wafer was used as a substrate for the needle array. Si needles were formed using anisotropic wet etching. We used hydrazine (N₂H₄) and TMAH (tetramethylammonium hydroxide) as etching solutions to improve the density of Si needles. At first, a Si wafer patterned by a SiO₂ mask was etched in the hydrazine solution at 115°C. Subsequently, etching employing the TMAH solution at 95°C formed sharp needles. This two-step etching increased the needle density five times than that fabricated by TMAH alone. After the sharp Si needle array was fabricated, through-holes were engraved to extract the blood from the back side of the Si wafer. A plasma-etching technique was employed to fabricate through-holes with a high aspect ratio. An electroplated Ni pattern performed a low erosive mask for the deep Si etching. At first, reversal hole patterns were photo-printed on a thick resist (SU-8) coated on the wafer backside. A Ni layer was then electroplated using a conductive Au/Cr layer. Finally, the holes were fabricated employing inductive coupled plasma (ICP) with SF₆ gas. After plasma etching was finished, the Ni mask with thickness of 100 μm was not removed. In addition to mask pattern for plasma etching, this thick Ni layer played a role of improvement of strength of the Si needle array chip for practical use of the blood collection.

3. Results and Discussion

Figure 2 shows a SEM image of the Si needle array chip fabricated by above process shown in Fig. 1. The height of Si needles is 500 μm. This height of Si needles are higher than the depth of epidermis (200 μm) and shorter than that of inner skin (2 mm). A (411) plane forms walls of sharp needles whose a top angle of needles is 42 degrees.

The blood was tried to collect from capillary vessel using the Si needle array chip. When we only pushed the Si needle chip on a human skin, we could not collect any blood,
Nevertheless, the length of Si needles seems to be long enough to pierce into a human epidermis, under which capillary vessels are present in inner skin. We therefore used a spring power and a vacuum force. Figure 3 shows an apparatus for blood drawing from capillary vessels. It is possible to decrease pressure in the tube of this apparatus by the pump power (see Fig. 8). Figure 4 shows a method of the blood collecting. While collecting of blood from capillary vessels, a human skin was exhausted by the pump power. This method utilizing both spring power and vacuum force enabled us to extract the blood from capillary vessels. Figure 5 shows the blood soaked from capillary vessels when the Si needles are pierced into a human skin using this apparatus. When bleeding, we did not feel any pain because of short height of Si needles. Figure 6 shows amount of bleeding as a function of piercing velocity of needles. The higher the needling speed became, the more amount of blood was shed. Necessary volume for a blood test on biochips is from 1 to 4 μl in our healthcare chip. Above a needling speed of 8 m/s, we can collect necessary amount of blood by using this painless Si needles. Figure 7 shows a photograph of the Si needle chip after bleeding. We did not find any crack for Si needles. This Si needle array chip was strong enough to apply to practical use of the blood collecting. This type of blood collector that has multiple needles has an advantage to diminish damage for human body in comparison with a single needle collector. Since total amount of blood is drawn from many cuts of the human skin when multiple needles are employed, each cut of skin can be diminished. Although scars for the blood collection remained even after a few days when the single needle was used to collect 1 μl blood, scars of skin pierced by this Si array chip to collect 1μl blood disappeared within a few days.

The whole blood has to be separated to blood cells and plasmas for the diagnostics. For the goal,
the Si needle array chip was combined directly with the PET chip on which a U-shape channel for centrifugal separation of the blood was fabricated. Figure 8 shows an illustration of the needle array chip fixed on a PET chip for the centrifugal separation and an apparatus collecting the blood sample. The bled blood was drawn into the PET chip by the vacuum power. Figure 9 shows a photograph after centrifugal separation of the blood on the PET chip. One can see that only blood cells are stored a pocket located at the middle of the U shape channel.

4. Conclusions

A painless extraction of the blood from capillary vessels using dense sharp Si needles fabricated on a Si chip employing alkaline wet and dry etching methods and subsequent separation to plasmas using the centrifugal channel chip combined to the needle Si chip have been developed. To reduce scars on the skin still, it is necessary to increase the density of the Si needle more.

References