DETECTION OF METALLIC ELEMENTS IN A SINGLE CANCER CELL USING MICROFLUIDIC DEVICES COUPLED WITH ICP-MS

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ABSTRACT

This paper presents a new single cancer cell analysis technique to combine microfluidic devices with inductively coupled plasma-mass spectrometry (ICP-MS). Inherent signals of cancer cells were quantitatively evaluated by launching the cells into ICP-MS via the microfluidic devices.

KEYWORDS

Single Cell Analysis, ICP-MS, PDMS.

INTRODUCTION

Single cell analysis technology has received much attention because of its capability of high accurate and quantitative analysis for each cell. Cells, which have a risk to be cancer cells, have the potential to change the inertial amount of metallic elements [1], and this slight variance are anticipated to be innovative biomarkers for an early cancer diagnosis. In this study, we fabricated the microfluidic devices to make cancer cells keep in line, analyzed behaviors of these cells under high-speed camera, and finally, launched those cells into ICP-MS via a nebulizer. The outline for the new single cell analysis system, and the design of microfluidic devices are shown in Figures 1(a) and 1(b), respectively.

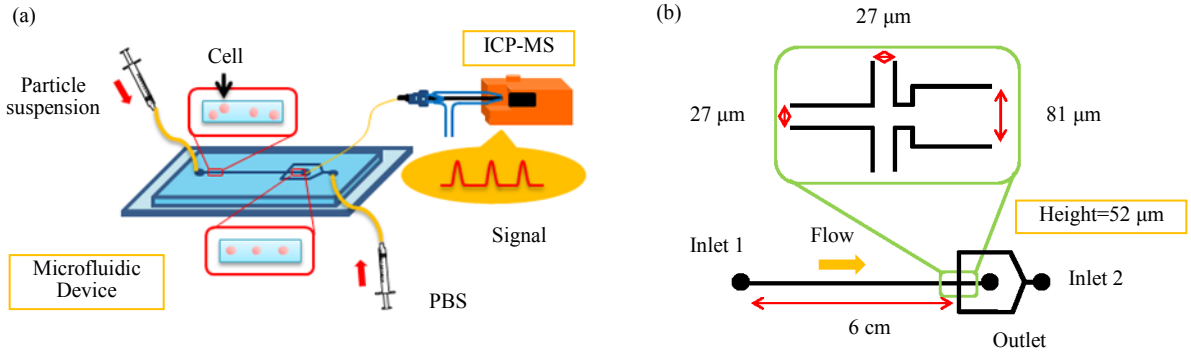

Figure 1 (a) Schematic of the system for single cell analysis. Cells inside microchannel were kept in line and launched to ICP-MS. (b) Details of the microchannel design; it had a high aspect ratio. Particulate solution and PBS were introduced from inlet 1 and 2, respectively.

Inside microchannels with high-aspect ratio, particles are caused to align into two evenly-spaced streams (Figure 2(a)). We combined this self-organized alignment with sheath flow, and forced cells to make an array with equal intervals. A photograph of fabricated microfluidic devices which were made by poly(dimethyl siloxane) (PDMS) and glass was shown in Figure 2(b). In Figure 2(c), flow rates for appropriate sheath flow were examined, and an optimum condition seemed to be lower one.

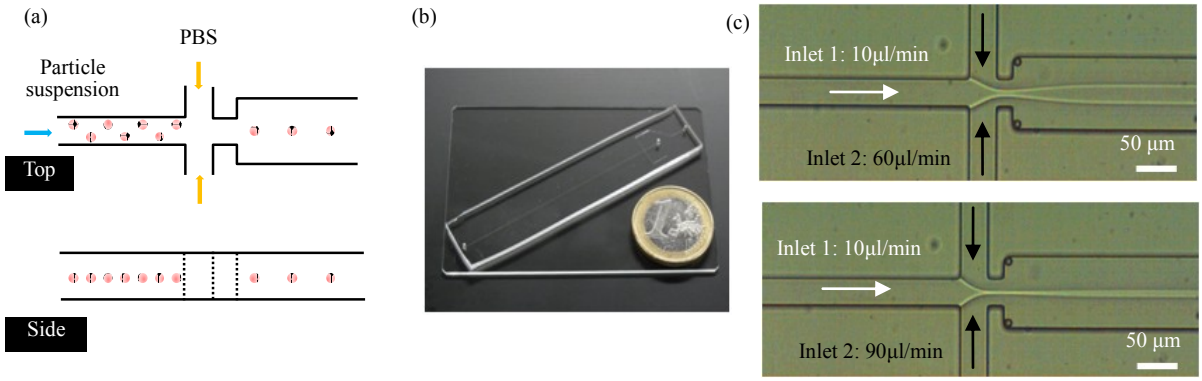

Figure 2 (a) Expected behavior of particles inside the microchannel (upper: top view, lower: side view) (b) Photograph of the fabricated microfluidic device. (c) Effect of flow rate in inlet 2 on sheath flow behaviors.

EXPERIMENT

We designed and fabricated some microfluidic devices using soft lithography and PDMS. Microbeads and cancer cells were introduced into these microfluidic devices, and those behaviors were captured by high-speed camera. PBS and suspension were introduced using syringe pumps. After that, we connected microfluidic devices into ICP-MS and measured the metallic elements. We used capillary tubes to connect an outlet of the microfluidic device into a nebulizer (details are shown in RESULTS AND DISCUSSION).

RESULTS AND DISCUSSION

Figure 3(a) shows the evenly positioned 10 μm microbeads. Sandwiched PBS flows forced microbeads to make the array with equal intervals inside a wider microchannel (Figure 3(b)), and the experimental setup using high-speed camera (8000 frames/s) is shown in Figure 3(c). Passing positions inside the wider microchannel were counted and made a histogram of microbeads' position inside the microchannel, leading to verification of an ability to make the array.

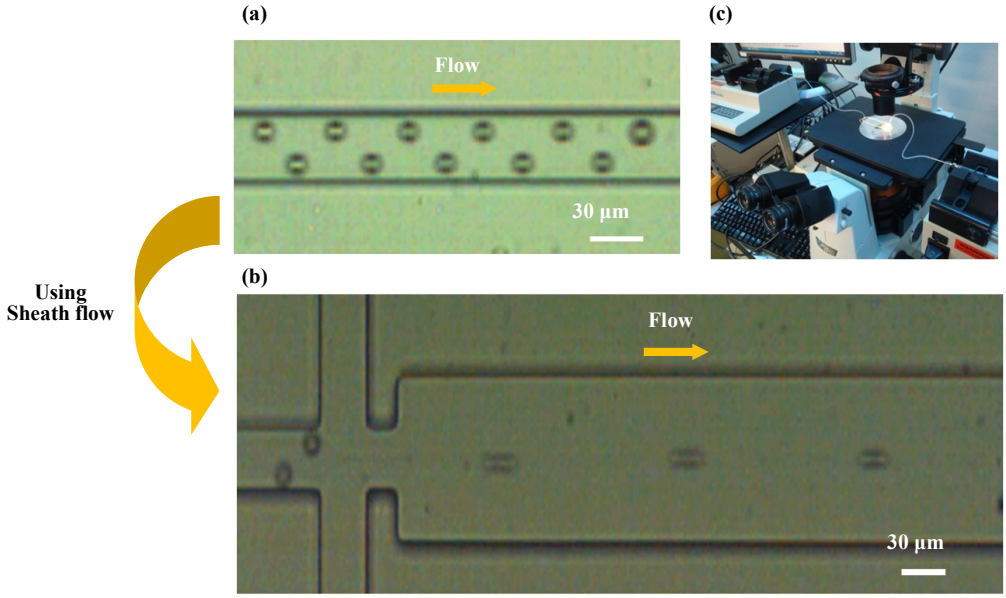

Figure 3 Micrographs inside microchannel. Particles' behavior was captured by high-speed camera. (a) Microparticles were arranged in two rows because of the balance of the two forces inside the high aspect-ratio microchannel. (b) Microparticles were arranged in a row by sandwiched PBS flows. (c) Photograph of experimental setup.

And also, human lung cancer cells (H1299) were introduced into these devices and in the same way as described above, these cells were forced to make the array inside the microchannel by sheath flow forces (Figure 4; flash photography, at intervals of 45 ms). The phenomenon performed here, *i.e.*, making the array of cells with equal intervals inside microfluidic devices, are of great importance, because the line of cells will make steady signals with periodic pattern, resulting in distinguish between healthy cell signals and cancer ones.

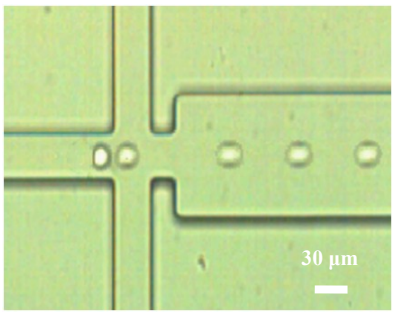

Figure 4 Flash photo of a cancer cell in the microchannel.

After making the array of cells with equal intervals inside the microchannel, we connected microfluidic devices into ICP-MS. Detail of the connection between the microfluidic device and ICP-MS is shown in Figure 5. We used capillary tubes to connect an outlet of the microfluidic device into a nebulizer, which can continuously launch the cells into ICP-MS because it does not have any drains. Magnesium signals, which should be derived from cancer cells, were measured by ICP-MS and represented.

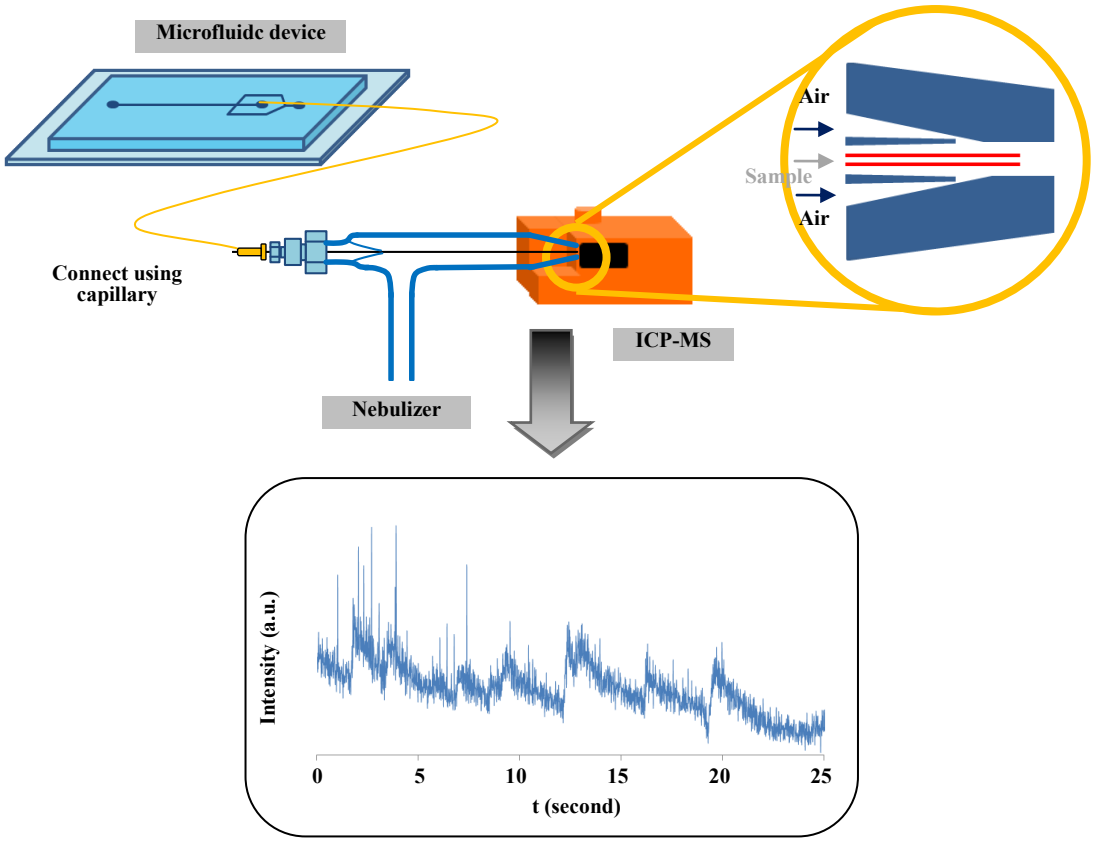

Figure 5 H1299 were introduced into the microfluidic device and launched to ICP-MS. The microfluidic device and ICP-MS were connected with capillary and nebulizer. A structure of the nebulizer is shown in the upper middle. Magnesium signals, which might be derived from cancer cells, were measured.

CONCLUSIONS

We succeeded to make microbeads keep in line into the microchannel. Magnesium signals, which might be derived from cancer cells, were measured by ICP-MS. If we measure all metallic elements included a cell, our developed technique would have a potential to be an innovative cancer diagnostic method.

ACKNOWLEDGEMENTS

This research was supported by the Japan Society for the Promotion of Science (JSPS) through its "Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program)".

REFERENCE

[1] "Metal Contents in the Liver of Patients with Chronic Liver Disease Caused by Hepatitis C Virus," Masaaki E, Hiroyuki F, Ryoji H, Masaharu Y, Nobuyuki S, Hiromitsu S, Fukuo K, Masae Y, Oncology, **65**; 323 (2003)

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