

Ferrohydrodynamic Separation of Circulating Tumour Cells



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Background & Motivation

Circulating Tumour Cells (CTCs)

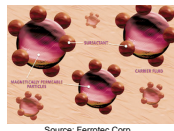
- CTCs are cancer cells that are shed from primary tumours and travel through the bloodstream to other organs.
- About 1-100 CTCs are found in 1mL of peripheral blood.
- Separation of CTCs is essential as they serve as a liquid biopsy target for cancer diagnosis (eliminating the need for painful biopsies), genotyping and prognosis, as well as a key factor in making therapeutic decisions.

Microfluidic Devices

- Simple and inexpensive means of separating CTCs.
- Provides high throughput and high separation efficiency.

Ferrohydrodynamics

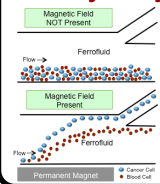
Ferrofluids



- Colloidal suspensions of magnetic (iron oxide) nanoparticles.
- The nanoparticles are covered by either electrostatic or steric surfactants to keep them apart.

- Ferrofluids have high initial magnetic susceptibility and high magnetization allowing for fast manipulation of non-magnetic objects in them leading to high separation throughputs.

Ferrohydrodynamic Separation



- Negative magnetophoresis
- Magnetic buoyancy force
- Hydrodynamic viscous drag force
- Size-based separation
- Label free, low cost

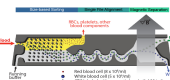
Existing Works



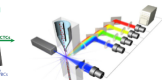
Source: www.ctc-lab.info
CellSearch by Veridex
 • Only FDA approved device.
 • CTC capture is based on EpCAM expression.
 • Expensive antibodies needed.
 • Separation takes several hours.
 • Antibody staining kills cells.



Source: Lenhof, Anal. Chem.
Acoustophoresis
 • CTC separation using acoustic radiation force.
 • Blood lysis required.
 • Low throughput.

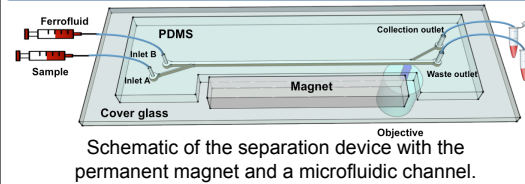


Source: Ottewill, Sci. Transl. Med.
CTC-iChip
 • CTC separation using magnetophoresis.
 • Expensive magnetic beads for tagging cells needed.
 • Low purity of negative depletion (0.1%).



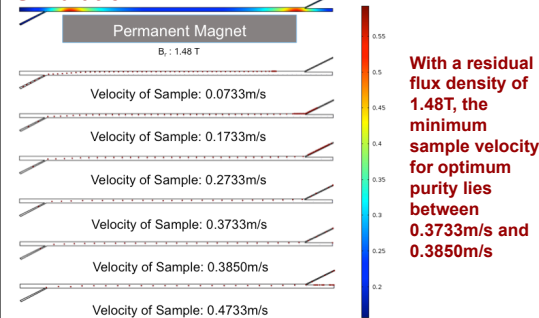
Source: Invitrogen
Fluorescence Activated Cell Sorter (FACS)
 • Flow cytometry using fluorescent lights.
 • Large and expensive system.

Experimental

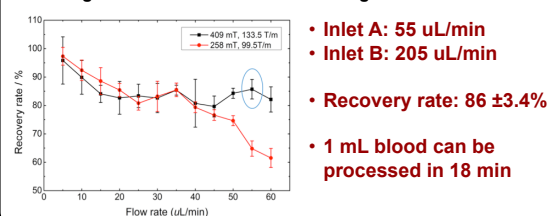
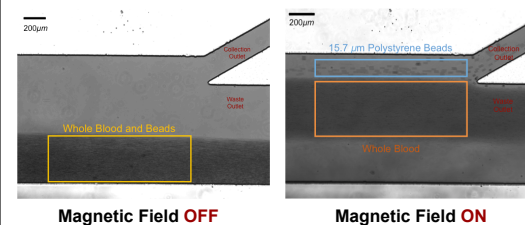


Results

Simulation

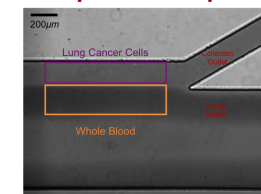


Calibration



Results

CTC Separation Experiment



- Inlet A: 50 uL/min
- Inlet B: 160 uL/min
- 1 mL blood can be processed in 20 min

Conclusions & Future Work

Advantages Over Other Devices

Our microfluidic chip addresses the limitations of other separation techniques with its low cost of production (~\$2 per device), high throughput (86 ± 3.4%) and high efficiency.

Future Work

Future work will include adjusting the device dimensions and magnetic field gradients for even more efficient separation and higher throughputs, lower costs, and ease of use by physicians. We also plan on testing the device on human cancer specimens.

- A higher throughput, which entails shorter processing time, could be achieved with multiple channels and more magnetic field gradients.
- Low cost and ease of use are needed to make the device available in low resource settings. The magnet could be embedded in the device to eliminate the need for a microscope, and a pressure difference applied in place of a syringe pump.

Acknowledgements:

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