Low-Cost Ethyl Cellulose Injector for Cervical Pre-Cancer Ablation in Low and Middle Income Countries

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Statement of Purpose: Cervical cancer impacts about half a million women annually, with an over 50% mortality rate[1,2]. Of these 270,000 deaths, about 87% have been reported in low and middle-income countries (LMICs) largely due to lack of access to crucial resources needed to diagnose and treat cervical pre-cancer[5]. This discrepancy highlights the need for low-cost, sustainable options for cervical cancer prevention in LMICs. Recent studies have found promise in ethyl cellulose ethanol (ECE) as an affordable biomaterial for ablation of cervical pre-cancer[3]. ECE holds advantages over conventional pure ethanol ablation, as it is known to form a gel in aqueous environments, resulting in sustained, localized treatment of the pre-cancerous lesions[4]. To enable clinical translation of ECE, a handheld injector is needed to control the needle placement and ECE injection through a speculum. An initial prototype of this device has been developed (**Figure 1**), featuring a 3 mL reservoir driven by a low-cost lead screw motor. However, ECE's viscous nature renders the low-cost lead screw motor unreliable as a driving mechanism. This study characterizes the pressure required to drive ECE to develop a more reliable device suited to the needs of LMICs.

Figure 1. CAD rendering of the existing lead screw-driven ECE injector prototype.

Methods: For clinical trials, a three-needle system is needed to reduce treatment time and optimize coverage. An apparatus driven by a Harvard Apparatus PHD Ultra Series syringe pump was used to determine the pressure. The upstream pressure was measured using a Honeywell TruStability pressure transducer (HSCDANN060PGSA3) and an Arduino Uno microcontroller. The system was first flushed with pure ethanol, then primed with ECE to eliminate air within the system. During the priming process, no needles were used, and the pressure was recorded to reflect any flow resistance posed by the system itself. During trials, five trios of 23G, 1.25" needles (BD PrecisionGlide BD305120) were attached and tested at a flow rate of 30mL/hr (10mL/hr per needle[3] Mueller et al.) with a 6 mL target volume which is required to reach steady state flow during ECE delivery. ECE was dispensed into open air during these trials.

Results and Discussion: The pressure profiles obtained during the five trials and the priming process are depicted in **Figure 2**. The priming pressure did not exceed 1 kPa, except for at minutes 7 and 9.5 where pressure spiked to approximately 1.5 kPa. This is thought to be due to the apparatus being disturbed during the process. Overall, the back pressure posed by the system was found to be negligible at such a low flow rate. Trials 1-4 exhibited a mean maximum upstream pressure of about 50±1.34 kPa. During Trial 2, a rapid pressure drop was observed at about 7 minutes which was recovered by the end of the trial. This was caused by bubbles introduced by user error before the trial. The pressure profile obtained in Trial 5 never exceeded 40kPa, which is likely the result of an air leak at the interface between the transducer and the system's tubing. This is corroborated by the notable decline in pressure that begins about 11 minutes into the trial. The trials' varying initial pressures are likely due to varying preparation times between trials, which was dependent on the user's ability to change needles. It is suspected that the gradual increase in pressure before reaching steady state for all of the trials is due largely to the compliance of the system's tubing.

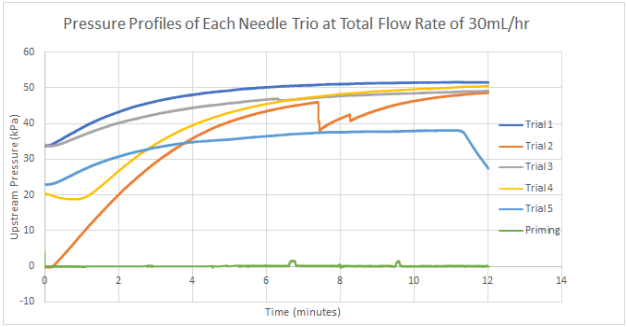

Figure 2. Pressure profiles for trials 1-5 and the priming process.

Conclusions: The pressure profiles obtained in trials 1-4, suggest that 50 kPa is needed to drive ECE through 23G 1.25" needles. Further experiments will be conducted investigating injection of ECE into tissue mimicking phantoms and swine cervices, to observe the impacts of these media on back pressure. Additionally, the results of trials 2 and 5 suggest that the test apparatus and protocol should first be revised for reliability. This work will lead to a multi-needle speculum-compatible injector for reliable delivery of ECE into the cervix and ultimately for treating women with cervical pre-cancer treatment in LMICs.

References

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