Sonopill: A Platform for Gastrointestinal Disease Diagnosis and Therapeutics

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INTRODUCTION

Gastrointestinal (GI) disease is recognised as a significant public health issue due to the growing number of patients diagnosed with colorectal cancer, coeliac disease and inflammatory bowel conditions such as Crohnôs disease. Endoscopy or colonoscopy is often used to image the GI tract to confirm diagnosis. However, while early detection is vital in cases of cancer as it increases the likelihood of survival, colonoscopy can induce discomfort in patients, reducing their willingness to undergo the procedure, delaying detection and treatment. Another disadvantage is that significant parts of the small bowel cannot be easily viewed as standard endoscopic imaging is limited to the upper GI tract and colonoscopy to the terminal ileum and below

More than one million patients have benefitted from capsule endoscopy (CE) since it emerged as a diagnostic tool over 10 years ago [1]. However, as shown in Table I, many of the commercially available CE tools utilise only visual imaging, limiting inspection to the mucosal surface. There is therefore room for innovation, with one route being the introduction of additional modalities so that the full potential of CE can be realised [2].

Ultrasound diagnosis and therapy are important goals of the Sonopill programme through integration in a capsule of the same physical volume as that used in video CE. Secondary modalities being developed for further integration are based on pressure, pH, temperature and chemical sensors. This development is being supported by pre-clinical work to demonstrate the complementary nature of multimodal imaging by ultrasonic and optical means in translational studies. The integration of these capabilities brings challenges and opportunities in a range of areas such as ultrasound device, sensor and systems design, microengineering, packaging and positioning and localisation as well as identifying routes to translation into clinical practice. This paper discusses some of these challenges and provides a brief overview of the work done to date.

MATERIALS AND METHODS

As shown in Figure 1, the Sonopill programme principally aims to achieve two demonstrator devices, ERIC (Epithelial Research Imaging Capsule) and CAIT (Capsule for Autonomous Imaging and Therapy), both intended to exceed the capabilities of existing capsules.

ERIC is a diagnostic capsule for imaging and sensing along and below the mucosal surface of the GI tract. Ultrasound is one of the main diagnostic imaging modalities, working in conjunction with visual imaging. It is safe and works in real time and is therefore already incorporated many endoscopic tools with miniaturised devices to fit within small volumes [3]ï[5]. It is also inexpensive to produce transducers, a vital factor for

Table I: Comparison between some commercially available capsule endoscopes and Sonopill

Brand	**Medtronic**			**Endo-capsule**		**Medimetrics**	**Sonopill**	
Model	SMARTpill	ESO2	COLON2	EC1	EC1-S10	Intellicap	**ERIC**	**CAIT**
Length (mm)	26	26	31.5	26	26	26.7	**30**	**30**
Diameter (mm)	13	11	11	11	11	13	**10**	**10**
Imaging (mm)	N/A	CMOS Image Sensor				N/A	**CMOS Image Sensor, High resolution ultrasound**	
Drug Delivery	No	No	No	No	No	Yes	**No**	**Yes**
Sensors	Pressure, pH, Temperature					pH	**Capability for pH, pressure, chemical, temperature**	

disposable devices such as CEs. However, its key ability is that it can image beneath the surface of the tissue, complementing visual imaging and improving early diagnosis of submucosal neoplasms amongst others.

Ultrasound can also act as a therapeutic treatment, either through direct tissue ablation using high intensity focussed ultrasound or through sonoporation to increase cell permeability for improved drug uptake [6]. These technologies, as well as other therapeutic methods, are being investigated for incorporation into CAIT.

The development of ERIC and CAIT makes the related challenges of positioning and localisation, already encountered by other CEs, even more acute. Therapeutic capsules will require accurate knowledge of the location of treatment sites detected by ERIC as well as the ability to resist the peristaltic forces of the gut that might otherwise move it during treatment. The ability to reorient the capsule would also improve diagnosis, allowing sites of interest to be investigated carefully and repeatedly. The development of the positioning system faces multiple challenges including the need to withstand the corrosive environment of the stomach to get to the small bowel and enhanced miniaturisation to allow sufficient space for imaging and therapeutic payloads while still being able to generate sufficient motive forces.

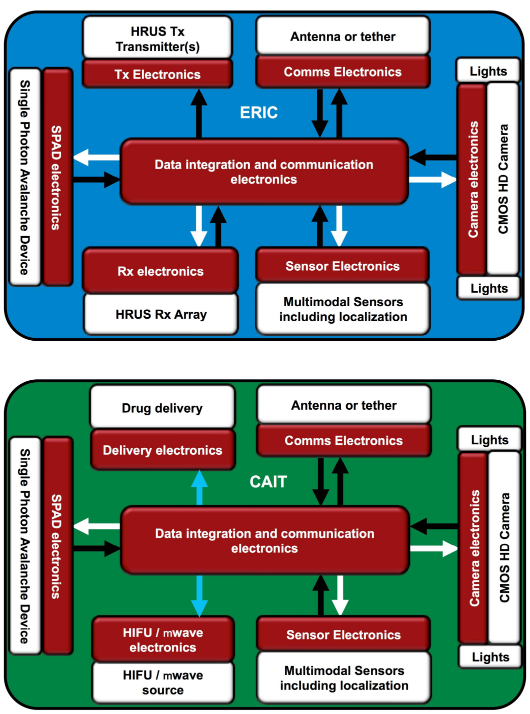

Fig. 1: ERIC (top) and CAIT (bottom)

Wireless communications is another challenge. Preliminary investigation of integrated antenna approaches has shown promise, but low efficiency [7] compared with imaging needs (~ 1 MB per frame). To mitigate this, as well as power consumption concerns, accelerometers will be integrated into the final design to allow the active components to be shut-down during slow movement and to complete data transmissions.

RESULTS

Currently the Sonopill programme has developed several reduced functionality, tethered ñpathfinderò pills to allow various sensing and therapeutic modalities and other systems such as communications to be independently tested before integration into the more functionally complex ERIC and CAIT demonstrators. These simpler pills will be used for translational studies *in vivo* in the near future.

CONCLUSION AND DISCUSSION

Reported cases of GI disease are growing worldwide and CE is increasingly used as a means of diagnosis. However, it is an immature technology in many realisations, open to further innovation and integration to provide new diagnostic and therapeutic tools as well as new avenues of research. In the Sonopill programme, ultrasound imaging and other clinically useful sensing modalities are being integrated into ERIC and new therapeutic methods are being investigated for CAIT. However, challenges such as positioning and localisation will need to be overcome to fully realise the goal of autonomous, steerable, wireless CE.

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