Biopsy channel of the endoscope as a potential source of infectious droplets during gastrointestinal endoscopy

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ABSTRACT (word count 250/250)

Background and aims: During endoscopy, droplets with the potential to transmit COVID-19 are known to emanate from a patient's mouth and anus, but they may also be expelled from the biopsy channel of the endoscope. The main goal of our study was to quantify droplets emerging from the biopsy channel during clinical endoscopy.

Methods: A novel light scattering device was used to measure droplets emanating from the biopsy channel. An endoscopy model was created, and *in vitro* measurements were carried out during air insufflation, air and water suctioning, and the performance of biopsies. Similar measurements were then made on patients undergoing endoscopy, with all measurements taking place over two days to minimize variation.

Results: During *in vitro* testing, no droplets were observed at the biopsy channel during air insufflation, or air and water suctioning. In 3/5 cases, droplets were observed during biopsies, mostly when the forceps were being removed from the endoscope. In the 22 patients undergoing routine endoscopy, no droplets were observed during air insufflation and water suctioning. Droplets were detected in 1/11 patients during air suctioning. In 9/18 patients undergoing biopsies and 5/6 patients undergoing snare polypectomies, droplets were observed at the biopsy channel, mostly when instruments were being removed from the endoscope.

Conclusions: We found that the biopsy channel may be a source of infectious droplets, especially during the removal of instruments from the biopsy channel. When compared with droplets reported from the mouth and anus, these droplets were larger in size and therefore potentially more infectious.

Keywords: COVID-19; droplets; biopsy channel.

INTRODUCTION

It has been recognized that the main transmission pathways of the severe acute respiratory syndrome coronavirus 2 (COVID-19) are through droplet and aerosol transmission[1,2]. Numerous procedures in the healthcare setting, such as gastrointestinal endoscopy, have been categorized as aerosol generating procedures[3]. We recently showed that both upper endoscopy and colonoscopy procedures are capable of producing droplets much larger than aerosols[4]. Since droplet volume scales with the cube of the droplet diameter, these large droplets have the potential to carry a much higher viral load and expose healthcare workers to an increased risk of viral transmission. The positioning of the droplet measuring device in our previous study allowed us to observe droplets emanating from either the patient's mouth or anus. We found a marked variation in the number of droplets produced by different patients during endoscopy, a variation that we could not completely explain by procedure duration, patient coughing, or use of a facemask. We hypothesized that the mouth and anus may not be the only source of droplets during endoscopy procedures, and that the endoscope biopsy channel may also be source. We therefore sought to conduct clinical measurements and *in vitro* simulations to determine if the biopsy channel could be a potential source of droplets. To evaluate the overall transmission risk provided by the biopsy channel, the quantity and size of the emitted droplets were compared with our previous study.

METHOD

A novel light scattering device capable of detecting and sizing fast-flying droplets was used for this study. The portable system was specifically designed to measure droplets during clinical endoscopy and has been described in detail elsewhere[4]. Briefly, droplets cross an expanded laser beam, and the angular scattering pattern that they produce is imaged using a primary charge-coupled device (CCD) camera. This scattering pattern is unique for droplets of different diameters and can be used to determine the droplet size. A secondary CCD camera is used to visualize the droplets and airflow is maintained with a fan. The entire system is contained within a 3D printed case, which allows no light to escape, making it safe for the clinical environment. A diagram of the system in the clinical setting is shown in Fig. 1, where the laser path, droplet path and device positioning are illustrated.

Given the limitations with preexisting data on quantification of droplets emanating from the biopsy channel during endoscopy, we started our experiment with hypothesis-generating in vitro simulations. The goal of our in vitro simulations was to determine if droplets were expelled from the biopsy channel. If we found evidence of droplet expulsion, we planned to quantify both the number and size of the droplets, along with identifying endoscopic manipulations that were most likely to result in droplet expulsion. Based upon clinical practice, we decided to test the following manipulations: air inflation and suction, water suction, and passage of instruments like forceps and snares in-and-out of the biopsy channel. We determined that our in vitro results would inform our clinical measurements and that we would perform similar measurements during routine clinical endoscopy, focusing on the manipulations that resulted in the greatest droplet expulsion. An a

priori sample size calculation was not possible given the absence of such data in the literature.

In vitro simulations

In vitro simulations were carried out to assess droplet expulsion from the biopsy channel during inflation and suction manipulations. We also sought to determine if there was an association between the length of time these manipulations were performed and droplet production. A large plastic bag with a partially filled beaker of water was used to simulate the gastrointestinal tract (Figs. 2A and B). The endoscope was inserted into the plastic bag and the bag was then sealed around the endoscope. The positioning of the device in relation to the endoscope is illustrated in Fig. 2A. To simulate upper endoscopy, we tested the following manipulations: (1) air inflation, (2) air suction, and (3) water suction. During the first round of measurements, we insufflated air into the plastic bag for 5 seconds while we measured droplets emitted from the biopsy channel. This was repeated 5 times, and the average of 5 droplet measurements was computed. Similar measurements were then performed for air suctioning and water suctioning. The second round of measurements was the same, except each manipulation was measured for 10 seconds. To determine if there was a change in the quantity or size of droplets emitted after the biopsy valve had been pierced with a biopsy forceps or other instrument, we pierced the biopsy valve twice with a forceps and repeated all measurements described above. Finally, to simulate the performance of a biopsy, polypectomy, etc., a biopsy forceps was inserted through the endoscope and then removed. Droplets were measured during the entire insertion

and removal of the biopsy forceps. The positioning of the device for the biopsy simulations is illustrated in Fig. 2C.

Clinical measurements

Twenty-two patients undergoing routine endoscopy procedures were enrolled in the study and the study was performed in accordance with the Beth Israel Deaconess Medical Center Institutional Review Board guidance. Given that temperature and humidity can impact the size profile of droplets, all procedures were measured in a single procedure room over two days to minimize variation. Furthermore, all procedures were performed by a single endoscopist to limit variation in technique. Measurements were taken during any endoscope manipulation that was deemed to produce an increased risk of droplet emission via the biopsy channel. The main manipulations that we investigated were air inflation, air suction, liquid suction, and the performance of biopsies/polypectomies. All procedures in the clinical and *in vitro* studies were performed using Olympus GIF-HQ 190 upper endoscope or Olympus PCF-H190L colonoscope.

RESULTS

In our *in vitro* simulations, no droplets were observed during air inflation, air suction or liquid suction, regardless of the manipulation duration or whether the biopsy valve had been previously pierced. However, droplets were detected in three out of the five biopsy simulations, with the normalized droplet incidence time plotted in Fig. 3A. A value of 0 corresponds to forceps insertion, while a value of 1 corresponds to forceps removal. It was observed that all droplets had normalized

incidence times greater than 0.94, suggesting that the removal of the forceps from the endoscope may provide the highest risk of droplet production. The size distribution of the droplets measured in the simulations is given in Fig. 3B, where the majority of droplets were between 55 μm and 85 μm. The mean ± SD temperature and humidity for the *in vitro* simulations was 21.8 ±0.1 C and 58.9 ±1.8 %, respectively.

The details of the procedures and measurements performed on the 22 patients who underwent endoscopy are provided in Table 1. The following endoscopic procedures were performed: upper endoscopy (n = 15), colonoscopy (n = 8) and pouchoscopy (n = 1). Air insufflation, air suction, and water suction were performed in 11 of 22 patients. During these manipulations, droplets were observed at the biopsy channel in only one patient, and this was during air suction. No droplets were detected in any of the other patients during air insufflation, air suction, or liquid suction. Biopsies were performed in 18 patients and droplets at the biopsy channel were observed in 9 patients (50%). A snare polypectomy was performed in 6 patients and droplets at the biopsy channel were observed in 5 patients (83%). One patient underwent placement of a naso-jejunal feeding tube. The tube was inserted through the biopsy channel of the endoscope and no droplets were observed during the insertion.

The total droplets measured for each manipulation type is given in Table 2, along with the average size and size range. The average number of droplets measured for each manipulation is illustrated in Fig. 4A, with polypectomies providing the largest average droplet number. While the entire forceps removal process was measured during both the biopsies and polypectomies, it was observed

that the majority of droplets came at the very end of the process, similar to the *in vitro* simulations. The size distribution of the droplets measured during all endoscope manipulations is shown in Fig. 4B. The mean ± SD temperature and humidity for the measurements on day 1 was 20.3 ±0.3 C and 63.7 ±1.1 %, respectively, while the mean ± SD temperature and humidity for the measurements on day 2 was 22.3 ±0.6 C and 30.9 ±2.9 %, respectively.

DISCUSSION

To our knowledge, this is the first report of measuring droplets expelled from the biopsy channel during clinical endoscopy. Observing and measuring droplets in clinical practice is technically challenging because most commercial devices are too bulky for the clinical setup and would interfere with the endoscopist. More compact systems cannot measure fast-flying droplets, and most lack the ability to distinguish liquid droplets from solid particles. Our group was the first to report on measuring droplets emitted from a patient's mouth and anus during upper endoscopy and colonoscopy[4]. Unexpectedly, in that study we found a large variation in the number of droplets produced by different patients undergoing endoscopy. Our present study suggests that some of that variation may be explained by droplets that were released from the biopsy channel during biopsy and polypectomy procedures.

In our current study, almost all droplets observed were detected during the biopsy/polypectomy procedures, mostly when the instrument was being removed from the endoscope. Droplets were observed in 50% of the patients undergoing biopsy procedures and 83% of the patients undergoing snare polypectomy

procedures. While the number of biopsy and polypectomy procedures in our study is too small to draw firm conclusions, it could be possible that the blunt plastic tip of the snare catheter may cause a larger perforation in the biopsy valve diaphragm compared to the metal biopsy forceps, resulting in an increased risk of droplets escaping from the biopsy channel. Compared to our previous measurements of droplets emanating from the patient's mouth and rectum, the droplets measured at the biopsy channel had a larger size profile. Most droplets emanating from the patient's mouth and rectum had diameters between 40 μm and 50 μm, whereas most droplets emanating from the biopsy channel had diameters between 65 μm and 145 μm. This is important given that the potential viral load of the droplet is proportional to the droplet volume, which is critical for understanding the transmission risk posed. In terms of quantity, we measured slightly more droplets emerging from the biopsy channel during upper endoscopies and colonoscopies, compared to our previous measurements of droplets emanating from the patient's mouth or rectum (4.1×10^{-2} mm^{-2} vs. 2.8×10^{-2} mm^{-2} and 4.0×10^{-2} mm^{-2}, respectively). However, given the positioning of the device, we expect that the biggest source of droplets is still the patient's mouth or rectum. To avoid interfering with the endoscopist, our previous measurements only sampled a small portion of the emission cone. When measuring droplets at the biopsy channel, the device could be placed much closer, and consequently, a much larger portion of the emission cone could be measured.

Our clinical measurements and *in vitro* simulations showed good agreement in terms of droplet potential and droplet timing. In the *in vitro* simulations, we found that the seal provided by the biopsy channel valve was robust and no

droplets emanating from the biopsy channel were detected during air insufflation or air and water suctioning. No droplets were noted even after the biopsy channel valve had been previously pierced. In terms of the biopsy simulations, droplets were observed in three of the five simulations, with the majority of droplets again detected when the biopsy forceps was being removed from the endoscope. The clinical measurements and *in vitro* simulations produced a different droplet size distribution, with larger droplets observed in the clinical measurements. One possible reason for this difference is that pure water was used for our *in vitro* simulations. While the size distribution was different, our results suggest that in vitro simulations could be useful for preliminary testing of any devices designed to reduce droplet exposure. While the same type of biopsy channel valve was used for all procedures in the clinical and *in vitro* experiments, it is possible that the type of endoscope and patient characteristics may impact size and quantity of droplets.

Results of our study have important implications for endoscopy in general, and not only within the context of COVID-19. A study by Johnson et al. found larger than expected exposure to biological contaminants to an endoscopist's face during routine endoscopy[5]. They estimated a contamination occurrence rate of 5.6 per 100 half days of endoscopy to the endoscopist's face, and of 3.4 per 100 half days of endoscopy to any healthcare member within 6 feet of the endoscope. While our measurements were not made near the endoscopist's face, we show that potentially infectious droplets could be launched during the forceps removal process. In another study, Vavricka et al. collected air samples close to the biopsy channel of the colonoscope in patients undergoing routine colonoscopy[6]. Compared with the beginning of the day, they found an increase in the air bioburden in the endoscopy

room after colonoscopies were performed. The highest air bioburden was detected when forceps were being removed from the colonoscope. The simple process of applying air suction with the colonoscope while the forceps were being removed decreased the bioburden by 50%, but the bioburden was still above baseline. In a study using an experimental model, Keil et al. demonstrated droplets of 0.1 – 1.1 mm diameter emanating from the biopsy channel at a velocity of up to 0.9 m/s only when a forceps was present within the biopsy channel[7]. No fluid particles were released without the presence of the forceps in the biopsy channel. Results of these studies, along with ours, suggest that biological contamination during endoscopy of both personnel and their surroundings is more common that recognized, and may in part occur while removing instruments from the biopsy channel of the endoscope.

The emergence of highly transmittable SARS-CoV-2 variants, including in those who have been fully vaccinated, makes it ever more important that we mitigate all possible sources of contamination during endoscopy[8,9]. Several investigators have proposed devices to reduce contamination during biopsies. Keil et al. showed in an experimental model that wrapping a protective cover made from a surgical cap around the biopsy channel eliminated the release of potentially infectious fluid particles[7]. Akahoshi et al proposed placing a vinyl bag over the biopsy channel, but did not study the efficacy of this approach[10]. Others have proposed various box-shaped shields placed around the patient's mouth and endoscopy to minimize contamination[11-14]. Since the highest risk of droplet production appears to be during removal of the forceps, we propose that having the assistant cover the biopsy channel opening with a cloth gauze while pulling the

forceps out of the endoscope may be sufficient to reducing droplet production. However, we have not studied the efficacy of this approach, but it will be the subject of broader future studies investigating the efficacy of various shielding devices for endoscopy.

While our current study provides important data for future investigations, some limitations of our study warrant further discussion. First, we were unable to find existing data on the quantification of droplets expelled from the biopsy channel during clinical endoscopy. This did not allow for a sample size calculation for our study, and therefore our ability to draw firm conclusions is limited by our final study sample size. Second, we assessed droplet expulsion during air and water insufflation in only 50% of patients undergoing endoscopy. Instead, we focused on measuring droplets during the passage of instruments through the biopsy channel, as we found that this manipulation was most associated with droplet expulsion in our *in vitro* experiments. Third, we did not collect patient level data during our study and are unable to determine if droplet expulsion from the biopsy channel was affected by patient characteristics.

In conclusion, we found that in addition to the mouth and anus, droplets are expelled from the biopsy channel during endoscopy. When compared with droplets produced at the mouth and anus, droplets produced at the biopsy channel are larger in size and therefore potentially more infectious. The highest risk of droplet expulsion appears to be during the process of pulling the forceps out of the endoscope. Evidence-based approaches to mitigate this potential source of contamination are needed.

Patient	Procedure	Measurement	Patient	Procedure	Measurement
1	Colonoscopy	AS, AI, WS, Snare (x2)	13	EGD	Biopsy (x3)
2	EGD	AS, AI, WS, Biopsy (x3)		Colonoscopy	Biopsy (x1), Snare (x1)
3	EGD	AS, AI, WS, Biopsy (x3)	14	EGD	Biopsy (x3)
4	EGD	AS, AI, WS, Biopsy (x2)		Colonoscopy	Snare (x1)
5	EGD	AS, AI, WS, Biopsy (x3)	15	EGD	Biopsy (x3)
6	EGD	AS, AI, WS, Biopsy (x3)	16	EGD	Biopsy (x2)
7	Pouchoscopy	AS, AI, WS, Biopsy (x3)	17	EGD	Biopsy (x4)
8	EGD	AS, AI, WS, Biopsy (x3)	18	Colonoscopy	Biopsy (x3)
9	Colonoscopy	AS, AI, WS, Biopsy (x3), Snare (x2)	19	Colonoscopy	Snare (x1)
10	EGD/NG	Tube insertion	20	EGD	Biopsy (x3)
11	EGD	AS, AI, WS, Biopsy (x3)	21	EGD	Biopsy (x2)
12	Colonoscopy	AS, AI, WS, Biopsy (x1)	22	Colonoscopy	Snare (x2)

Table 1. Clinical measurement information for 22 patients. Patients 1 to 12 were enrolled on day 1, while patients 13 to 22 were enrolled on day 2. EGD denotes esophagogastroduodenoscopy, while AS, AI and WS denote air suction, air inflation, and water suction, respectively.

Endoscope Manipulation	Droplet Number mm^{-2}	Average Size μm	Size Range μm
Air Suction	0.08	91	47 - 124
Biopsy	0.47	118	43 - 277
Polypectomy	0.35	109	47 - 176

Table 2. The total number of droplets, along with average size and size range, observed for each endoscope manipulation during air suction (11 patients), biopsies (18 patients) and polypectomies (6 patients).

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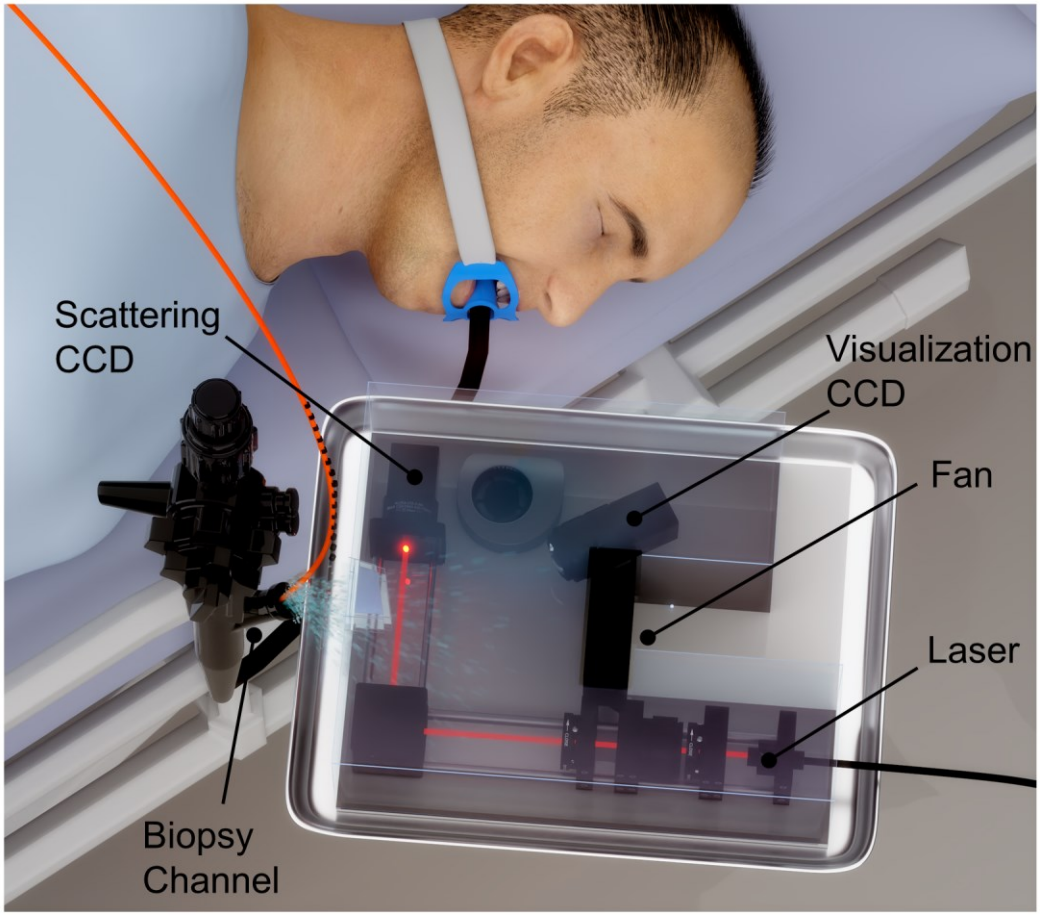

Figure 1. Portable light scattering device for measuring droplets expelled during clinical endoscopy. Positioning of the device in the clinic with the laser and droplet path clearly visible.

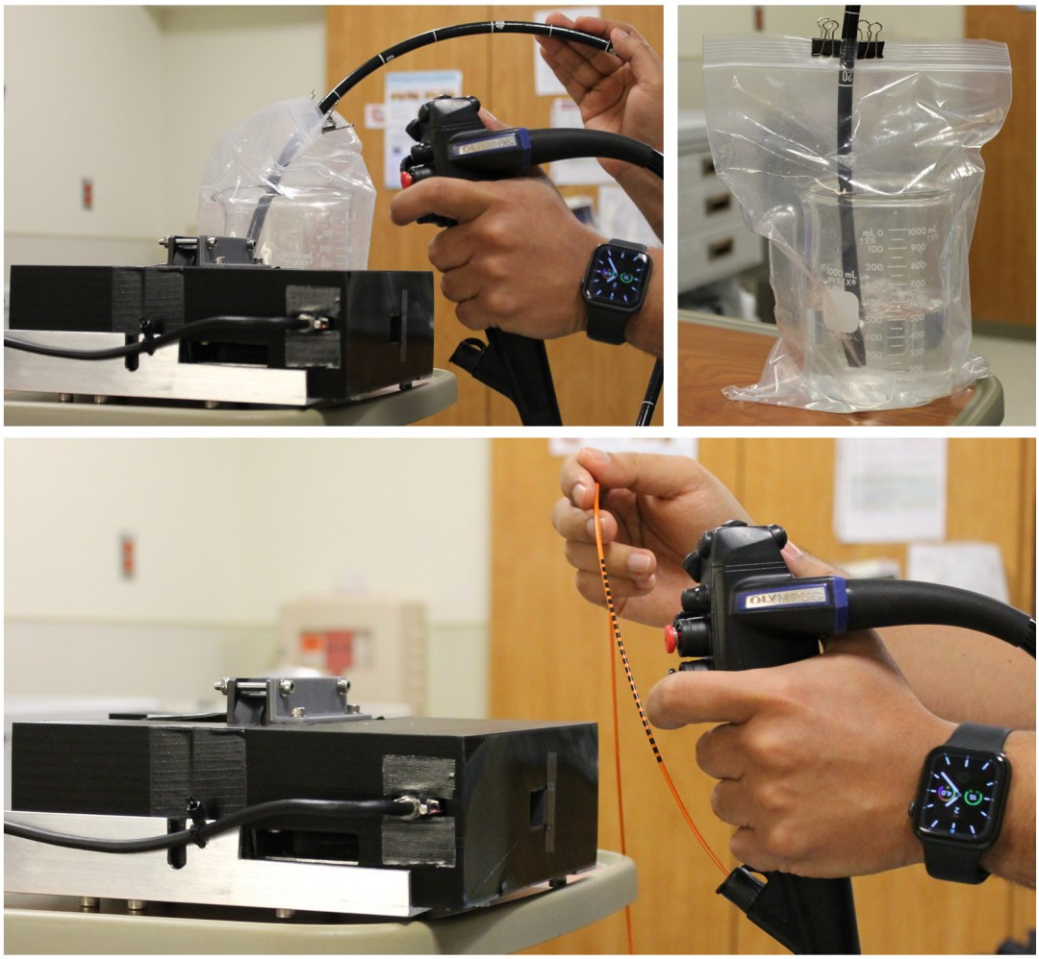

Figure 2. Clinical simulations. Positioning of the endoscope and device for the various endoscope manipulations (A). Endoscope end submerged in water (B). Positioning of the endoscope and device for biopsy simulations (C).

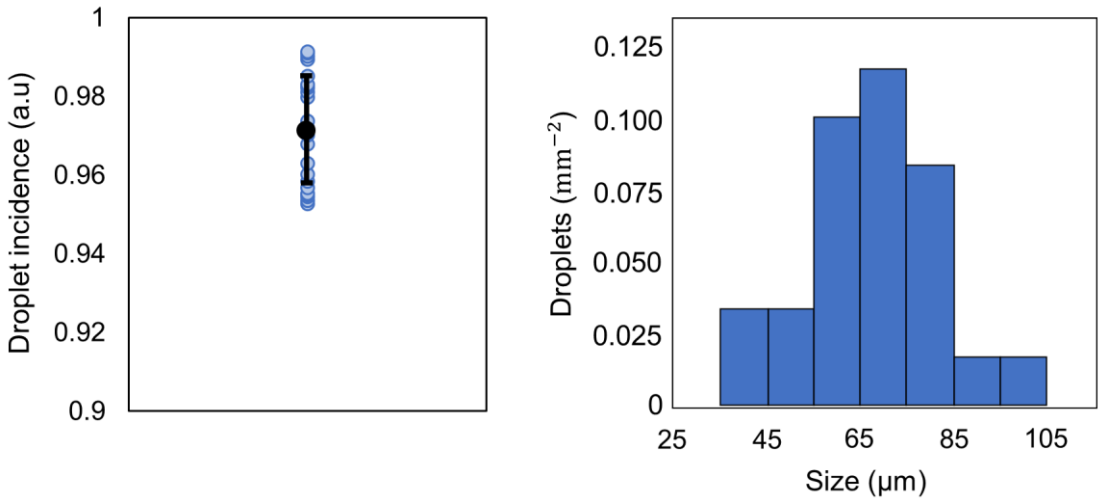

Figure 3. Droplets observed during *in vitro* simulations. Normalized droplet incidence time for biopsy simulations, with average and SD shown in black (A). Droplet size distribution for the *in vitro* simulations (B). a.u. denotes arbitrary units.

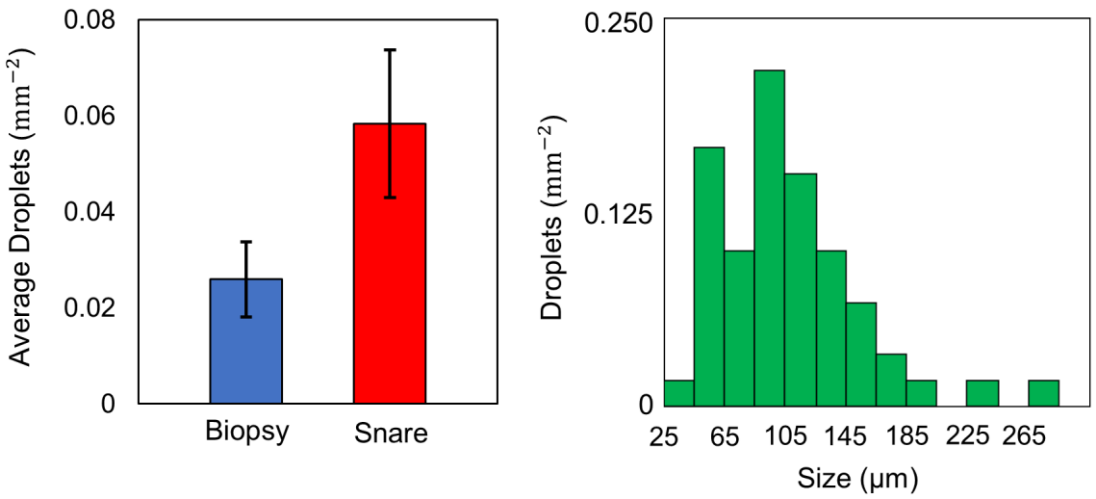

Figure 4. Droplets observed during clinical measurements. Mean number of droplets for each procedure. Error bars represent standard errors (A). Droplet size distribution for clinical measurements (B).

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