Bioinspired Spring-Loaded Biopsy Harvester—Experimental Prototype Design and Feasibility Tests

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Current minimally invasive laparoscopic tissue–harvesting techniques for pathological purposes involve taking multiple imprecise and inaccurate biopsies, usually using a laparoscopic forceps or other assistive devices. Potential hazards, e.g., cancer spread when dealing with tumorous tissue, call for a more reliable alternative in the form of a single laparoscopic instrument capable of repeatedly taking a precise biopsy at a desired location. Therefore, the aim of this project was to design a disposable laparoscopic instrument tip, incorporating a centrally positioned glass fiber for tissue diagnostics; a cutting device for fast, accurate, and reliable biopsy of a precisely defined volume; and a container suitable for sample storage. Inspired by the sea urchin's chewing organ, Aristotle's lantern, and its capability of rapid and simultaneous tissue incision and enclosure by axial translation, we designed a crown-shaped collapsible cutter operating on a similar basis. Based on a series of in vitro experiments indicating that tissue deformation decreases with increasing penetration speed leading to a more precise biopsy, we decided on the cutter's forward propulsion via a spring. Apart from the embedded spring-loaded cutter, the biopsy harvester comprises a smart mechanism for cutter preloading, locking, and actuation, as well as a sample container. A real-sized biopsy harvester prototype was developed and tested in a universal tensile testing machine at TU Delft. In terms of mechanical functionality, the preloading, locking, and actuation mechanism as well as the cutter's rapid incising and collapsing capabilities proved to work successfully in vitro. Further division of the tip into a permanent and a disposable segment will enable taking of multiple biopsies, mutually separated in individual containers. We believe the envisioned laparoscopic optomechanical biopsy device will be a solution ameliorating time-demanding, inaccurate, and potentially unsafe laparoscopic biopsy procedures. [DOI: 10.1115/1.4026449]

Keywords: laparoscopy, biopsy, optical biopsy, high speed, Aristotle's lantern

Background

Laparoscopy and Biopsy. Laparoscopy, minimally invasive surgery in the abdomen, is becoming increasingly more popular due to its capability to considerably minimize incision size, postoperative tissue trauma, and patient recovery time [1–5]. Yet, the advantages come at the expense of a limited site access and restricted tissue manipulation [2,6].

The state-of-the-art, minimally invasive biopsy methods [7] mainly involve needle biopsy, usually used for sampling thyroid, breast, and prostate tissue, and punch biopsy, used for sampling skin and bone tissue (Fig. 1) [8]. However, these biopsy techniques generally lack application versatility, mainly due to the limitations of the existing biopsy devices [9,10]. To illustrate, the biopsy needles have been designed and used for deep-tissue biopsy, thus rendering them inappropriate for peripheral intra-abdominal tissue sampling. Similarly, punches used for peripheral-tissue biopsy would be very limited in terms of use within the laparoscopic context with regard to speed or accuracy at a smaller scale, for instance. Furthermore, using a regular laparoscopic forceps or scissors for biopsy can likely result in tissue slip and, hence, insufficiently accurate tissue sampling with associated risks [11].

The need for greater accuracy, procedure reliability, time- and cost-efficiency, as well as minimizing potential handling hazards [9,12–14], e.g., cancer spread when dealing with tumorous tissue [15], calls for an alternative, more-robust biopsy technique combining a real-time tissue diagnosing technology with a precise, easily operable laparoscopic biopsy harvester. For clarification, the terms robust and robustness are used throughout this paper in the context of enhanced device capabilities and fitness for purpose while satisfying the aforementioned needs.

Combining Optical and Mechanical Biopsy. When it comes to endoscopic tissue diagnosis, there are various emerging technologies that could ameliorate lengthy pathological procedures by providing instant real-time in situ tissue analysis. Hence, pathology could be performed without the need for multiple discrete and lengthy operations—in other words, much more readily and thus supposedly at reduced costs. These diagnostic technologies incorporate a range of differing tissue-imaging techniques, usually using fiber optics as a signal carrier, and they are collectively designated as "optical biopsy" [14,16].

By incorporating the optical biopsy technology within a laparoscopic instrument and combining it with a mechanical tissue–removal device—a biopsy harvester—one could achieve greater robustness and time efficiency compared to the current standard. Normally, the retrieved biopsies (usually of indefinite volume and tissue properties) are sent to a lengthy pathological analysis and may require subsequent treatment of the patient after a couple of days or even weeks, either for more biopsy samples or for tumor resection. Naturally, apart from the obvious time delays, such a segmented and usually repetitive process can increase the risk of cancer spread. Instead, with an optomechanical biopsy harvester, one would be capable of an instant optical analysis in situ with the possibility of a precise tissue removal exactly at the analyzed site and all within a matter of seconds.

Problem Statement—Need for a Novel Optomechanical Biopsy Device. Current patented concepts of laparoscopic instruments combining glass fibers for optical measurements with tissue

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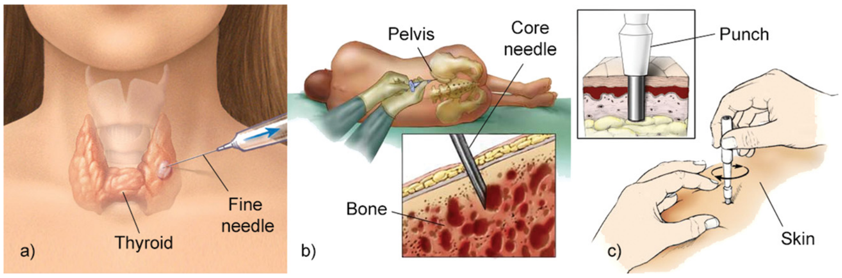

Fig. 1 Examples of contemporary biopsy techniques including (*a*) fine-needle aspiration, (*b*) core-needle biopsy, and (*c*) punch biopsy; adopted from Ref. [8]

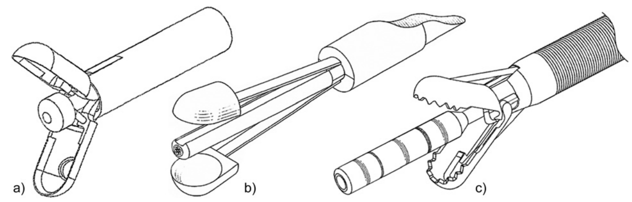

Fig. 2 Examples of laparoscopic optomechanical biopsy tip concepts patented by (*a*) Sharon et al. [17], (*b*) Whitehead et al. [18], and (*c*) Lacombe et al. [19]

manipulation devices (Fig. 2) [17–19] lack accuracy and practicality, mainly due to insufficiencies of their end effectors and their inappropriateness for accurate targeting and delicate tissue handling at smaller scale. As a consequence, such devices would be inadequate for performing the optical and mechanical biopsy operations in a reliable, accurate, and fast succession at the same location or in a single procedure. Hence, such device concepts were not considered for the envisioned laparoscopic application of optically analyzing and sampling the diseased internal abdominal organ and tissue surfaces.

Therefore, in order to enhance the contemporary laparoscopic biopsy procedures with robustness, accuracy, and efficiency, there is a need for a novel dexterous optomechanical biopsy device that would compensate for the aforementioned weaknesses of the state-of-the-art biopsy techniques, devices, and concepts.

Minimal Tissue Deformation Approach Towards Laparoscopic Biopsy. To outline the combination and incorporation of optical and mechanical biopsy in laparoscopy, one has to look at the fusion of these two technologies in a practical manner—from the perspective of reaching the targeted site and the means of tissue handling.

With a laparoscopic instrument, a surgeon can approach the targeted peripheral tissue either frontally or laterally [2]. Since tissue analysis and its subsequent accurate extraction are required, one has to reconsider the ideal approach to the tissue based on the design constraints of both the laparoscope and the imaging technology. Once a thick glass-fiber bundle of a large bending radius [20] is integrated into a long, slender tubular geometry of a laparoscope's shaft, the only possible way the fibers can then guide the signal is frontally and coaxially with the instrument itself. Furthermore, in order to ensure an accurate and rapid succession of actions at reduced complexity, the mechanical biopsy should follow the direction of the preceding optical measurements. Therefore, rather than analyzing and handling the targeted tissue separately or from different angles, a reasonable decision was made to enable performing both the optical and mechanical biopsy frontally and in a close succession.

One could successfully perform the mechanical biopsy at a high level of accuracy by ensuring a minimal deformation of the targeted tissue caused by the cutting device. As described in Fig. 3, this could be, in theory, achieved by compensating for the

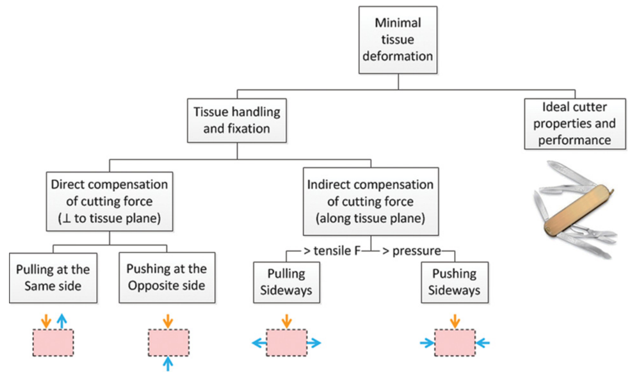

Fig. 3 The means of achieving minimal tissue deformation during frontal tissue penetration (compensation force, upward and sideways arrows, is described relative to the cutting-force vector, downward arrows)

frontal cutting force either directly or indirectly. Direct compensation would involve either pulling or pushing action perpendicular to the tissue surface and parallel to the applied cutting force vector. Indirect compensation would comprise a pulling action along the tissue surface, thus increasing the tissue's surface tension, which would ameliorate the cutting process. Alternatively, indirect compensation could also involve a pushing action parallel to the tissue surface, thus increasing the tissue's inner pressure, helping to make it more stable for the cutter penetration.

Nevertheless, from the design point of view, such tissue handling and fixation would most likely require auxiliary features in the laparoscope's tip, such as hooks or adhesives. On the other hand, the invasive tissue-tip interaction prior to the actual cutting operation could result in an undesired bias in the diagnostic readings—due to an impeded blood flow, for instance. Such additional auxiliary features would also result in higher design complexity or even design infeasibility, given the limited dimensions.

In order to simplify the method of achieving minimal tissue deformation as well as the laparoscope's tip design, a different approach would be required. Such approach would be to devise an idealized cutter capable of an effortless penetration at a minimal tissue deformation, solely thanks to its clever design, with no use of auxiliary features. Thus, design simplicity and robustness could be achieved while preventing any biasing tissue manipulation prior to the optical biopsy.

Objective—Design Requirements. The aim of this project was to design a simple, novel laparoscopic instrument tip of dimensions typical of a regular laparoscopic forceps, i.e., Ø 5 mm and 20–40 mm length [21]. Such a tip has to provide a central unimpeded Ø 2 mm lumen for a glass-fiber bundle for the optical analysis of superficial tissue properties. The optical analysis feature has to be supplemented with a compact frontally acting cutting device for fast, accurate, and reliably controlled mechanical biopsy of the analyzed superficial tissue. The biopsy sample of a precisely

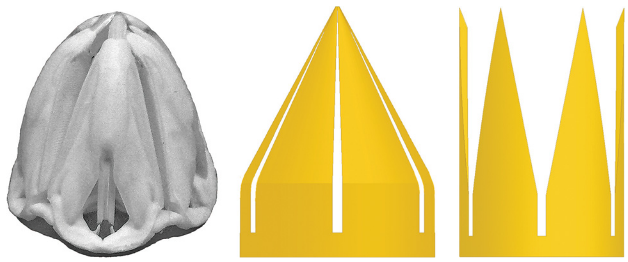

Fig. 4 Sea urchin's chewing organ, Aristotle's lantern—left—providing an inspiration to the biopsy harvester's crown-shaped collapsible cutter (collapsed—center, at rest—right)

defined tissue volume will also be kept and transported in an embedded sample storage container for further pathological analysis.

Method of Approach—Experimental Prototype Development

Design Inspiration and Cutting Principle. In pursuit of developing an ideal biopsy device, one might wonder how to combine a perfect tissue incision with biopsy retrieval in a single tool or procedure. Since accurate, laparoscopic, frontally acting biopsy harvesters of peripheral tissue do not yet exist, at TU Delft, we decided to search for an inspiration in similar approaches in nature. Therefore, we took a closer look at the sea urchin's clever chewing organ, Aristotle's lantern (Fig. 4, left) [22].

Aristotle's lantern is a relatively large and featureful structure, around 15 mm in height and diameter, consisting of five larger bones ending in a beak with five small pointy teeth, and it is actuated by a complex network of muscle tendons located within the sea urchin's bulky exoskeleton. The beak bites through and encompasses even a very tough material, e.g., corals, by pressing the mutually fitting teeth together by axial translation, due to the basal attachment of the muscle tendons [22,23]. More specifically, Aristotle's lantern is open when protruding outwards and closed when retracted inwards. As demonstrated by Giorgo Scarpa's bionic model of Aristotle's lantern [24,25], by this means, the sea urchin can simultaneously cut off and enclose its food in a seemingly unified and continuous motion. The capability of the simultaneous tissue incision and enclosure by axial translation exactly fits the envisioned biopsy harvester's functionality needs. This is due to the fact that the arising opportunity for a close succession of the optical and the mechanical biopsies could lead to an enhanced accuracy of the analyzed and sampled tissue.

Cutting and Harvesting Mechanism. Building on this principle, yet restrained by the limited laparoscopic tip dimensions, a round, crown-shaped collapsible cutter was designed (Fig. 4, right), physically resembling Aristotle's lantern and enabling simultaneous tissue incision and enclosure. Since any hinged features would likely lack sturdiness at this scale, not to mention their manufacturing feasibility, the cutter had to be designed thin enough as to allow the collapsibility of the blades and thus the enclosure of the sampled tissue. Six symmetrical blades were chosen as optimal both for manufacturing feasibility and for creating a seemingly straight blade cross section for easy inward bending, while keeping the blade profiles wide and strong enough to prevent outward bending when retracted.

Propulsion—Pilot Cutter Experiments. The sea urchin's beak geometry and working principle were recognized as essential for the envisioned biopsy harvester, combining frontal cutting with tissue encompassing. However, together with its muscle and tendon actuators, it is difficult to replicate in a miniature and simple form. Therefore, it has been decided to modify the crown-cutter's operation such that it would close automatically by forward propulsion. Furthermore, to gain further insight and inspiration on the means of the cutter actuation, an in vitro experiment was performed in the Tensile Testing Lab of our department. Its goal was to find out what forces such a cutter encounters during tissue penetration and to test its cutting capabilities. The crown-cutter was mounted in a clamp (Fig. 5, left) attached to a 1 kN load cell of a tensile tester Zwick/Roell Z005 (TÜV Nord AG, Hanover, Germany) and pushed vertically downwards into a single piece of chicken liver placed freely on a platform. This test was performed repeatedly at different locations on the liver. During the push-in tests, the forces exerted on the cutter were plotted against the increasing penetration depth at a sampling rate of 10 Hz and at push-in speeds 6, 12, 24, and 48 mm/s. The same protocol was followed with the cutting experiments performed on a single piece of chicken breast. The collapsing motion of the cutter blades was not yet taken into account in this experiment, i.e., the cutter stayed open.

The data from numerous push-in trials on chicken liver is plotted at every speed (ten trials per speed) and fitted with exponential curves for clear comparison (Fig. 5, right). Based on these force measurements, it was determined that the higher the push-in speed was, the lower the forces on the cutter or tissue were. It was also observed that, at higher speeds, the cutter penetrated the tissue effortlessly and with less visible tissue deformation, thus presumably leading to a more accurate biopsy. Compared to the chicken liver trials, the experiments with the chicken breast showed only a slight increase in the exerted forces on the tissue/cutter, yet the push-in speed increase showed the same trend (hence, not shown). It was therefore concluded that a plausible approach to a precise and accurate biopsy is high-speed cutting. Hence, we decided on

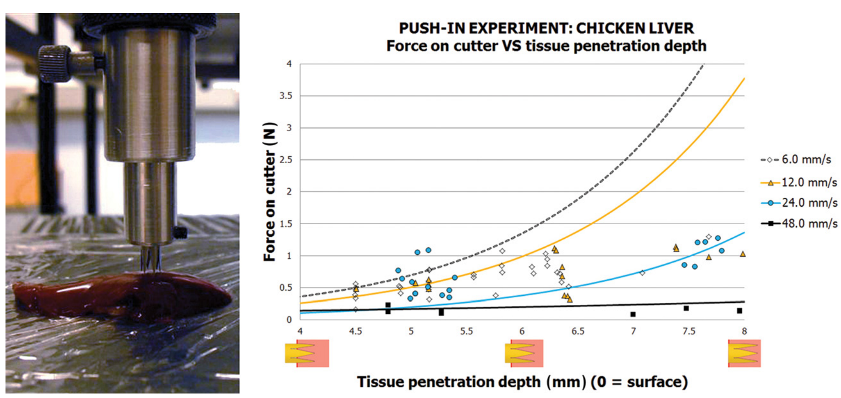

Fig. 5 Close-up of the pilot test setup, left, and the results of the in vitro push-in tests, right, performed with the crown-cutter on a chicken liver at push-in speeds 6, 12, 24, and 48 mm/s. For clarity, the data are presented from the penetration depth of 4 mm onwards, and they are fitted with exponential curves for easy comparison.

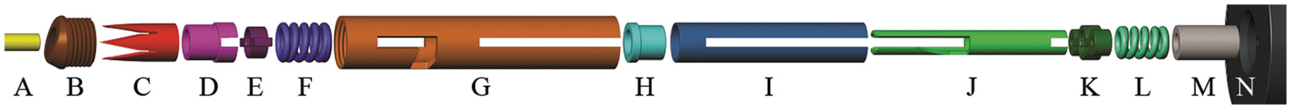

Fig. 6 Exploded view of the spring-loaded biopsy harvester design with its 14 components (A–N), showing their mutual axial alignment

the cutter's forward propulsion via a fast and strong compression spring.

Experimental Biopsy Harvester Design. The concept of a crown-shaped collapsible cutter propelled by a compression spring with an embedded glass-fiber bundle was determined. The next challenge was to incorporate these founding features into a laparoscope's tip design, which would also comprise a smart mechanism for cutter preloading, locking, and actuation. As the purpose of this prototype design was to test the cutter's functionality and feasibility, the biopsy harvester was initially designed without a removable container for sample transport.

The finalized prototype design, illustrated in Fig. 6, contains a collapsible crown-cutter (C, D, and E) that sits on a compression spring (F), with a tubular, Ø 6 mm and 30 mm-long outer shell (G) positioned around them. The tip accommodates an internally tapered screw-on cap (B), which serves to collapse the cutter blades into a cone-shaped sample storage container when pushed forwards through the tissue. Thus, a maximum biopsy volume and penetration depth are maintained, as they are defined solely by the angle of the internal taper and the cutter's geometry. The design furthermore features a central Ø 2 mm inner channel, suited for accommodating a glass-fiber bundle (A) and a smart mechanism for cutter preloading, locking, and actuation. Due to the small working space confined in between the Ø 2 mm central channel and the Ø 4.5 mm inner diameter of the outer shell, the tip comprises a compact sandwich construction of several tubular parts that slide over each other and operate the crown-cutter. A short-pinned sleeve (E) runs in a slot in the outer shell (G), which is shaped as a letter "J" in order to enable fast and easy cutter loading and locking. The compression spring is released by pulling a long inner sleeve (J) with a specially angled guiding slot. The angled slot translates the sleeve's pulling motion into a rotational motion of the pinned sleeve (E), turning the pins into the straight part of the J-shaped slot and rapidly releasing the spring from the compressed state.

The long inner sleeve (J) is fused with a short sleeve (K) featuring two round protrusions with holes. Bowden cables run through these holes with their outer coils pushing at the short sleeve (K) protrusions and their inner wires anchored in the base (N) (Fig. 9, left). By this means, the cutter can be actuated remotely by pulling the components (J) and (K) towards the base (N).

Fig. 7 Assembled biopsy harvester prototype manufactured nearly at real-scale, Ø 6 mm, (top) also showing a fully closed crown-cutter (inset). Intermediate assembly (bottom) shows the outer shell, the assembled inner working mechanism, and the glass-fiber dummy.

Experimental Biopsy Harvester Prototype. The experimental biopsy harvester prototype (Fig. 7) was manufactured from stainless steel and mounted to an aluminum base suited for clamping in a tensile testing machine. The axisymmetric six-blade crown-cutter was electric discharge machined (EDM) from a thin extruded steel tube Ø 4.3×0.15 mm and equipped with a 20 deg inner bevel. All other components were machined via regular means of milling and turning, with the exception of several symmetrical slots and protrusions that had to be machined by the EDM as well. Components (J) and (K) were fused by the means of a heat-treated permanent metal glue.

Experimental Setup for Feasibility Tests. The experimental biopsy harvester prototype was firstly trialed and observed in free space in order to investigate the mechanism functionality in general. This was supplemented by footage of the cutter closure in free space taken by a high-speed camera Fastcam Ultima APX-RS (Photron USA Inc., San Diego, CA) at 30,000 fps.

For the purposes of the in vitro feasibility tests, the biopsy harvester was mounted on a 1 kN load cell of the tensile tester Zwick/Roell Z005 (TÜV Nord AG, Hanover, Germany) and tested on a single piece of chicken liver placed freely on a platform. The biopsy harvester was firstly brought as close to the tissue as possible, making a gentle tissue contact with its tip. This was followed by the rapid incision operation remotely actuated by the Bowden cables and performed repeatedly at 20 different locations on the liver. The cutting process was recorded at a sampling rate of 100 kHz with respect to the measured force on tissue/cutter over time.

Last, but not least, to verify the cutting consistency, the 20 biopsy samples were weighed on Scaltec analytical balance SBC 33 (Denver Instrument GmbH, Göttingen, Germany).

Results

General Prototype Functionality. The cutter preloading, locking, and actuation mechanism proved to work successfully and

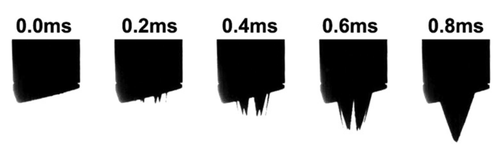

Fig. 8 High-speed camera snapshots of the rapid cutting process performed in 0.8 milliseconds

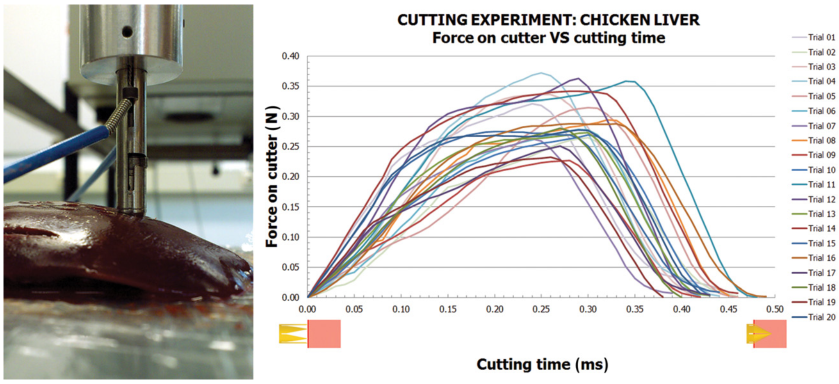

Fig. 9 Close-up of the Bowden cable-driven biopsy harvester testing setup, left, and the results of the in vitro cutting tests on a chicken liver, right, illustrating the forces exerted on the cutter during the rapid cutting process

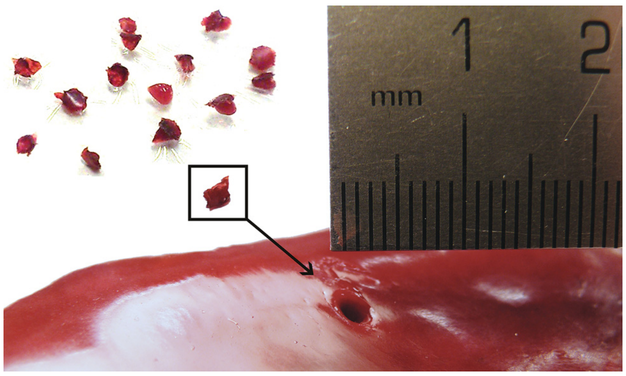

Fig. 10 Clean-cut conical biopsies of a chicken liver made with the bioinspired biopsy harvester

continues to function even after daily demonstrations, with no visible signs of plastic deformation or material fatigue. As shown by the inset in Fig. 7, the crown-cutter closes seamlessly, hence, it is capable of extracting an almost perfectly conical biopsy volume of about 9 mm^3 at most (estimated from geometry); this equates to 9.8 μg of liver tissue at the liver density of approximately 1090 kg/m^3 [26]. As observed from a sequence of snapshots (Fig. 8), the spring shoots the crown-cutter from open to closed position in 0.8 ms. At the cutter's axial travel of 4.4 mm, this equates to the cutting speed of 5.5 m/s.

Prototype's Cutting Performance and Feasibility Test. Using the experimental setup for feasibility tests (Fig. 9, left) discussed previously, a plot of force on cutter against the cutting time was generated (Fig. 9, right). The readings indicate that, only during the first 0.5 ms of the cutting operation, measurable forces can be registered—their maxima being in the range of just 0.23–0.37 N. As demonstrated in Fig. 10, the cutter managed to perform successful biopsies, rapidly sampling and storing conical tissue volumes while leaving clean round cuts as desired. Based on a pure observation, the 20 extracted liver samples were roughly consistent in terms of geometry and volume. Their further weighing revealed an average sample mass of $3.1 \pm 0.4\ \mu g$.

Discussion

Biopsy Harvester Highlights and Limitations. The experimental prototype of our novel, bioinspired, optomechanical biopsy harvester proved to work successfully. The success was demonstrated by the cutter's incising and collapsing capabilities enabling rapid sampling of chicken liver tissue of conical volume in vitro, while operating at low friction. The experimental prototype tests also showed repeatable flawless mechanical operation of the preloading, locking, and actuation mechanism. The desired functionality was achieved despite the amount of numerous miniature components—many of them on the verge of manufacturability.

The crown-cutter design proved to exert minimal forces on tissue during the rapid cutting process, barely reaching 0.4 N at the speed of 5.5 m/s. For the sake of comparison, a generic core needle biopsy gun operates at 30 m/s [9]. At the same time, the cutting process managed to deliver roughly constant results, both in terms of tissue sample shapes and sizes, with a standard deviation of the sample mass of only $\pm 13\%$. As revealed from the high-speed footage, the cutter takes 0.8 ms to fully close, even though the force plots indicate measurable forces only during the first 0.5 ms. A plausible explanation is that, as the cutter closes and becomes a pointy cone, the surrounding tissue is no longer pushed away along the cutter's motion vector, but rather sideways as it is ripped apart. Hence, no measurable force is registered during the last 0.3 ms of the cutting process, during which the cutter closes completely, sealing off the biopsy sample from the rest of the tissue.

Despite the successful sample retrieval and a visually seamless closure of the cutter blades, the liver tissue did not appear to be perfectly separated just by the cutting process itself. However, the full sample separation was effortlessly achieved immediately upon retracting the biopsy harvester from the site, thus breaking off the miniscule remaining connecting tissue. It was in fact observed that, since the EDM process easily melts very thin metal features, it caused the blades' tips to be mutually slightly unequal, introducing a modest clearance at the very tip of a closed conical cutter. Hence, sharpening would have to be performed separately, by turning for instance. This could explain the relatively smaller average sample size of approximately 32% of the maximum theoretically extracted biopsy volume of 9 mm^3. Nevertheless, both the perfect tissue separation and the sample volume maximization could be supposedly achieved by optimizing the cutter's blade bevel.

Future Work—Envisioned Instrument. As suggested, the next step would be a series of in vitro evaluations carried out on animal tissues with the objective of optimizing the cutter's incising and retrieving capabilities. More specifically, the research goals will involve optimizing the crown-cutter's blade bevel with regard to further minimizing the tissue deformation, maximizing the retrieved tissue volume, as well as achieving a perfect separation of the sampled volume from the tissue site just by the cutting process itself.

Further design modifications and division of the tip into a permanent and a disposable segment will enable taking of multiple biopsies, mutually separated in individual storage containers, suited for accurate and efficient pathological analysis. For surgical purposes, the individual segments will further have to be enclosed or sealed, so that no potential tissue entrapment could occur due to the slots or the protrusions.

The real-scale criterion of Ø 5 mm was not yet fulfilled, due to the removability feature of the screw-on cap requiring a thicker outer shell for thread. The cap in the final instrument would be permanently glued, soldered, or spot-welded to the outer shell, hence allowing it to be much thinner. In the end, the final real-scale Ø 5 mm partitioned device will be evaluated in vivo on small and large animals.

Conclusions

A Ø 6 mm, bioinspired, optomechanical biopsy harvester prototype was developed and tested in vitro on chicken liver using a universal tensile testing machine. In terms of mechanical functionality, the preloading, locking, and actuation mechanism as well as the cutter's rapid incising and collapsing capabilities proved to work successfully. The embedded crown-cutter enables rapid tissue incision and enclosure, highly accurate with regard to the preceding optical biopsy. The biopsy harvester features a Ø 2 mm lumen either for the purposes of the optical tissue analysis or for expanding its capabilities, e.g., flushing/suction channel or micrograsper. Further division of the tip into a permanent and a disposable segment will enable sampling multiple biopsies, mutually separated in individual containers. Once mounted on top of a laparoscopic instrument, the envisioned optomechanical biopsy harvester would provide an accurate, efficient, and comfortable solution towards ameliorating time-demanding, inaccurate, and potentially unsafe laparoscopic biopsy procedures with regard to peripheral tissue sampling.

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