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Elephas Live™ Edge: An Automated Cutting Instrument Used to Produce Live Tumor Fragments for the Assessment of Immunotherapy Response Ex Vivo

Purpose

This white paper introduces Elephas Live™ Edge, an automated cutting instrument used to precisely cut clinically relevant tissue form factors, such as core needle biopsies (CNBs), while preserving large contiguous areas of the native tumor microenvironment (TME).

Introduction

Problem Statement

Components of the native TME play a critical role for characterizing immune checkpoint inhibitor (ICI) response[1–6]. However, many approaches to predict response to ICI do not maintain an intact live native TME (eg, histological or genetic biomarkers) reducing their accuracy potential. It has been shown that ex vivo models may more accurately predict response to ICI when larger, more contiguous areas of the native TME are maintained, allowing assessment of ICI response under conditions most closely resembling the patient's tumor[7]. However, such models require large amounts of tumor tissue collected via resections to address challenges of tumor heterogeneity.

CNBs are collected through standard of care diagnostic procedures in clinical settings where patients are likely to receive immunotherapy. Therefore, the ability to efficiently process CNBs and assess their response to ICI ex vivo greatly enhances the practical potential of the Elephas Live™ Platform for conducting ex vivo functional precision medicine. To maintain ex vivo culture over ~72 hours, the biopsy tissue needs to be of a size that does not impede nutrient flow into the tissue core, yet maintains a large area of contiguous TME. To achieve this balance, the CNBs must be cut uniformly and this poses a technical challenge for automation due to the size and delicate nature of CNBs. Elephas Live™ Edge is an automated cutting instrument designed to overcome challenges associated with precisely cutting small tissue pieces, such as CNBs, while preserving large areas of native TME.

The Elephas Live™ Platform enables ex vivo profiling of live tumor tissue

The Elephas Live™ Platform enables ex vivo culture of live tumor fragments (LTFs) created from CNBs to assess tumor response to immunotherapy[8]. CNBs are cut into LTFs approximately 300 µm in thickness using Elephas Live™ Edge, an automated cutting instrument (Figure 1). LTFs are then encapsulated in a proprietary hydrogel (Elephas Live™ Protect) and treated using a sequential treatment strategy (Elephas Live™ Method) in which IgG control followed by ICI are added to the same well. Tumor response to ICI is then assessed by cytokine profiling.

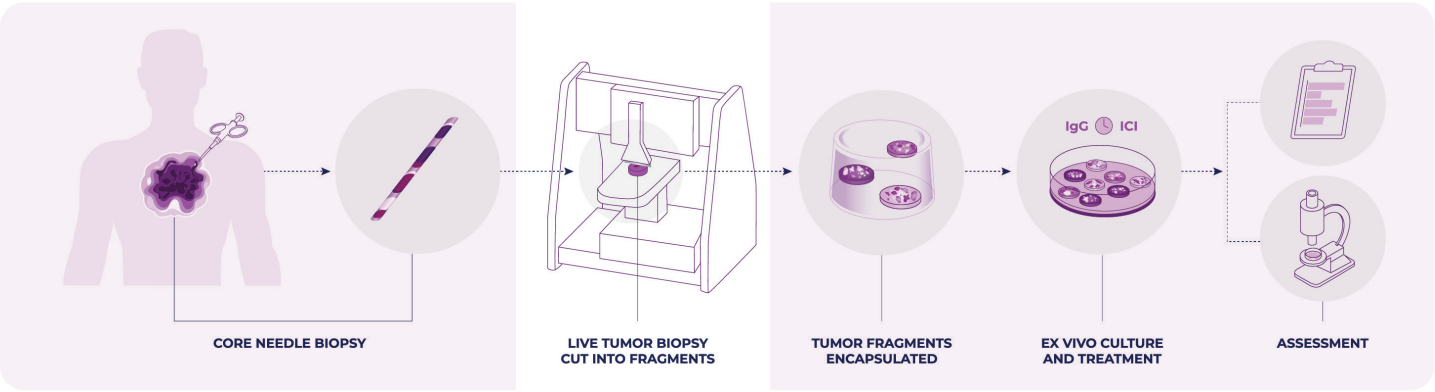

Figure 1. An overview of the Elephas Live™ Platform. LTFs from human CNBs are cut with Elephas Live™ Edge, encapsulated in Elephas Live™ Protect, sequentially treated with IgG control then ICI, and assessed for response.

Elephas Live™ Edge enables automated, precise cutting of small, delicate tissues.

CNBs are small pieces of tissue collected from a patient's tumor that range in size from ~1-2 mm in diameter, depending on the needle gauge (12-20 gauge) used for biopsy collection, and 3-20 mm in length depending on the tumor size and type. Cutting of this tissue poses challenges due to the range of size and delicate nature of the tissue. Placing the entire CNB into a single culture well would keep the largest contiguous area of the native TME intact and negate the need for tissue cutting; however, without cutting, the CNB becomes deprived of sufficient nutrients due to tissue thickness, making it more prone to necrosis. Elephas Live™ Edge is an automated cutting instrument that produces LTFs from CNBs as small as 20-gauge while maintaining an intact and viable TME, thus solving for current issues in biopsy processing (Figure 2). Even when CNBs are frail and delicate, automated cutting with Elephas Live™ Edge allows for greater precision in LTF shape and size that is challenging to achieve with hand cutting. Compared to hand cutting, Elephas Live™ Edge decreases the number of user touch points, increasing scalability and reducing inconsistency in sample processing.

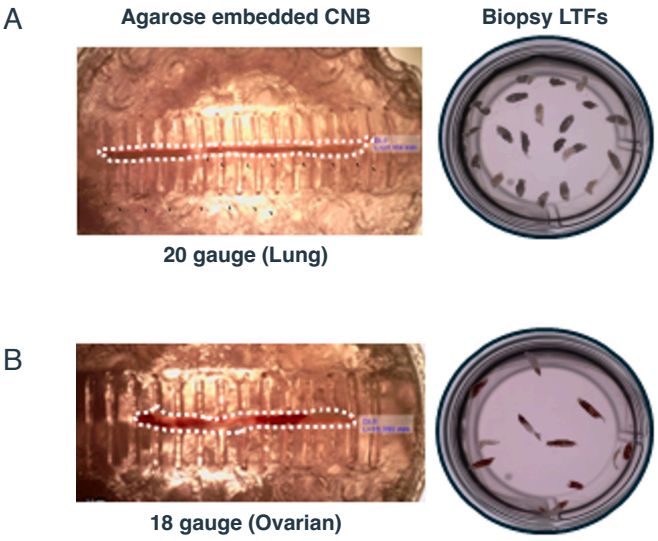

Figure 2. Representative images of CNBs cut on Elephas Live™ Edge. A) A 20-gauge Lung cancer biopsy embedded in agarose and the subsequent LTFs. B) An 18-gauge Ovarian cancer biopsy embedded in agarose and the subsequent LTFs.

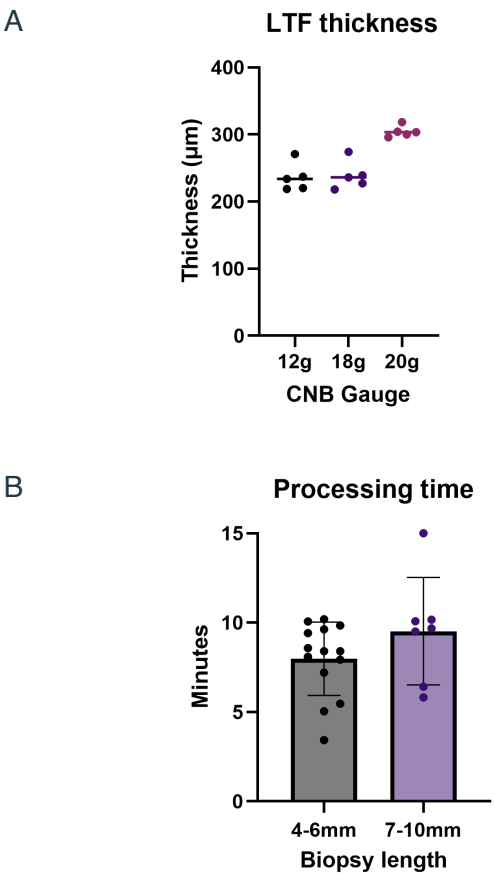

Figure 3. The Elephas Live™ Edge blade cuts consistently as it passes through the length of the gel mound. A) Consistent LTF thickness by biopsy gauge size. B) Processing time in minutes by CNB length (mm) shows that Elephas Live™ Edge cuts through the majority of CNBs within 5-10 minutes.

The Elephas Live™ Edge blade vibrates while sectioning to precisely and consistently cut through CNBs. Vibrating the blade while cutting prevents pulling, tearing, and deformation of the CNB that can occur when the blade is forced through the tissue[9,10]. The blade oscillates to generate oblique cuts with a uniform thickness of ~300 µm (Figure 3A). Optimal nutrient diffusion in tumor tissue occurs at distances less than 150 µm from capillaries[11]; tissue cut at a thickness of ~100 µm or less risks a decrease in cell viability and an increase in tissue damage, while tissue cut at a thickness greater than 300 µm results in poor nutrient diffusion[12]. Therefore, the thickness of 300 µm allows for the greatest amount of contiguous tissue to be cut without compromising tissue integrity, cell viability, and nutrient diffusion. Elephas Live™ Edge processes a single CNB in as little as 5 minutes, with processing times for most longer CNBs under 10 minutes (Figure 3B).

Elephas Live™ Edge maintains larger contiguous areas of the native TME and reduces cutting time compared to alternative cutting methods.

Alternative cutting methods include cutting a CNB longitudinally (0° angle) to produce thin sheets of tissue or perpendicularly (90° angle) to produce circular pieces of tissue. CNBs cut at 0° maintain more contiguous TME; however, more surface friction occurs between the blade and tissue, which results in breakage and poses a technical challenge for automated tissue cutting. Cutting at 90° yields more LTFs per CNB, but the LTFs consist of less contiguous TME (Figure 4A). At 20°, about 3.5 times more contiguous area of TME is maintained than tissue cut at 90° (Figure 4B). Thus, the 20° angle cut offers a balance between maintaining greater areas of intact TME and reducing tissue breakage while cutting.

Other drawbacks for cutting at a 90° angle include additional cutting of the tissue and extended cutting time. The duration of a 10 mm CNB cut lasts ~18 minutes and requires 29 cuts. However, cutting the same length CNB at 20° takes ~8 minutes for 13 cuts (Figure 4B). The decreased cutting time at the 20° angle allows tissue plating and processing to occur more efficiently than at 90°, which reduces a potential negative impact on viability and increases the scalability of tissue processing.

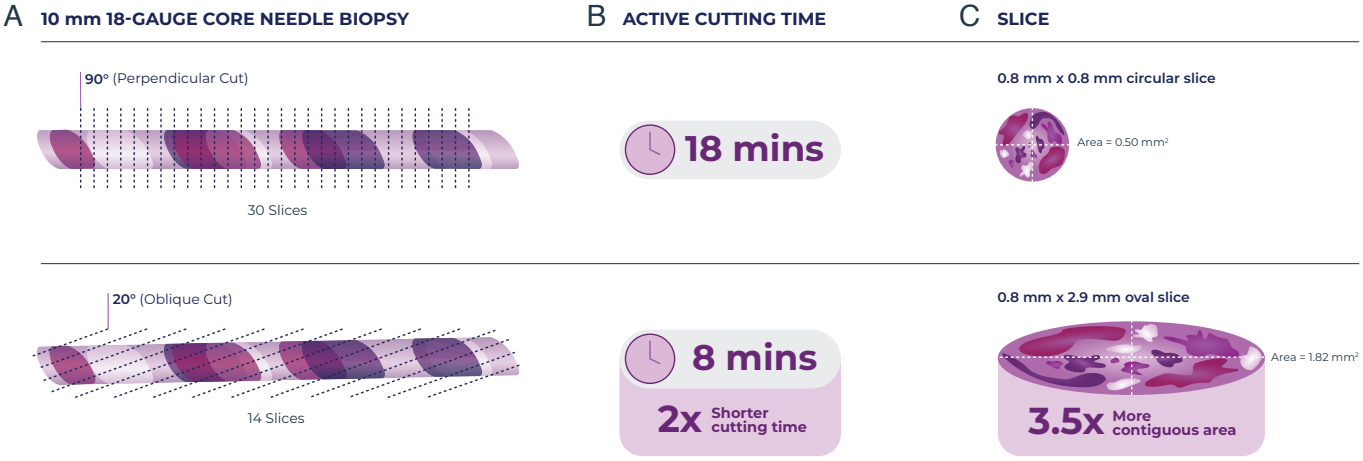

Figure 4. Cartoon drawings of CNBs depicting the cutting angles of 90° and 20°. A) The difference in the number of LTFs created from a 90° cut and a 20° cut on a 10 mm biopsy. B) CNBs cut at 90° take two times longer than CNBs cut at 20°. C) At 20°, 3.5 times more contiguous area is present in the LTFs compared to 90°.

Table 1 lists the estimates for the target total tissue per well for CNB LTFs cut at a 90° or 20° angle from samples collected by various needle gauges. The volume per fragment for CNBs cut at 20° is greater than 90° across all gauges (Table 1).

		Volume per fragment (mm^3)		Fragments per well		Total tissue volume (mm^3)	
Gauge	Inner diameter (mm)	90°	20°	90°	20°	90°	20°
12 g	2.159	1.140	2.980	5	2	5.702	5.960
14 g	2.109	0.603	1.580	9	3	5.429	4.739
16 g	1.194	0.339	0.887	16	6	5.429	5.320
18 g	0.838	0.166	0.439	33	12	5.486	5.270
20 g	0.603	0.085	0.219	64	25	5.429	5.470

Table 1. LTF characteristics and parameters for 12- to 20-gauge biopsies at 90° versus 20°.

LTF Cutting Process

Sample Collection

CNBs are received from patients as additional cores collected during standard diagnostic procedures and placed in a 15 mL conical tube containing transport media for processing on the Elephas Live™ Platform.

Sample Preparation

The CNB and media are then poured into the embedding mold (Figure 5A) where the excess media seeps through the drain holes on the bottom of the mold. Once the CNB is positioned horizontally and rests flush along the bottom of the mold, the user dispenses 7.5 mL of a gel (eg 37°C agarose) and firmly presses the sample mount into the embedding mold. The gel solidifies on ice for 5 minutes before loading the sample holder onto the Elephas Live™ Edge instrument (Figure 5B) at a 20° angle. The sample holder is tightened with the sample holder nut (Figure 5A) to stabilize the CNB embedded in the gel mound during cutting.

Elements of cutting on the Elephas Live™ Edge

The Elephas Live™ Edge blade holder consists of two components: the scoring blade and the collection blade (Figure 5C). The vertical blade, or the scoring blade, sections the tissue a total of 39 times in equal increments of 300 µm (Figure 2 and Figure 5D). The scoring blade travels down 3 mm as it oscillates with a peak-to-peak amplitude of 2 mm to create oval LTFs (Figure 5E).

The horizontal blade, or collection blade (Figure 5F), is positioned 0.5 mm above the bottom of the score depth. It approaches the sample at 12.5° to separate the tissue from the gel. The collection blade oscillates at a larger amplitude and slower frequency across 10 mm to fan out the LTFs as they release from the gel.

The collection blade, now holding the slices, moves to a position above the petri dish containing media. The end user slides the slices into the dish with a spatula.

Use for Elephas Live™ Platform

The LTFs are plated in a 24-well plate, encapsulated in Elephas Live™ Protect, and cultured for 72 hours to assess cytokines and predict response to ICI on the Elephas Live™ Platform.

Figure 5. Computer-aided design of the Elephas Live™ Edge cutting instrument and its consumables: A) the sample holder, B) the Elephas Live™ Edge instrument with the sample holder and blade mounted, and C) the blade holder with the collection and scoring blades. Animated images depicting the cutting process: D) the blade sectioning, E) an example oval LTF, and F) the collection cut.

Conclusion

Elephas Live™ Edge creates LTFs by precisely cutting CNBs while maintaining large areas of contiguous TME. Elephas Live™ Edge increases the throughput and scalability of CNBs processed on the Elephas Live™ Platform by automating and increasing the efficiency of the cutting process.

Learn more about how the Elephas Live™ Platform enables prediction of response to immunotherapy at **our website** and view additional resources highlighting Elephas Live™ Edge here:

Elephas Live Edge™ Video: Watch a short video of an animated demonstration of cutting on Elephas Live™ Edge

2025 AACR Poster: The Elephas Live™ Platform includes Elephas Live™ Edge–a bespoke instrument designed to cut live tumor biopsies into fragments

Journal of Translational Medicine Publication: A live tumor fragment platform to assess immunotherapy response in core needle biopsies while addressing challenges of tumor heterogeneity

References

1. Moldoveanu, D. et al. Spatially mapping the immune landscape of melanoma using imaging mass cytometry. *Sci. Immunol*. 7, (2022). **2.** Gil-Jimenez, A. et al. Spatial relationships in the urothelial and head and neck tumor microenvironment predict response to combination immune checkpoint inhibitors. *Nat. Commun*. 15, 2538 (2024). **3.** Wang, X. et al. Spatial interplay patterns of cancer nuclei and tumor-infiltrating lymphocytes (TILs) predict clinical benefit for immune checkpoint inhibitors. *Sci. Adv*. 8, eabn3966 (2022). **4.** Jiang, P. et al. Signatures of T cell dysfunction and exclusion predict cancer immunotherapy response. *Nat. Med*. 24, 1550–1558 (2018). **5.** Arlauckas, S. P. et al. In vivo imaging reveals a tumor-associated macrophage–mediated resistance pathway in anti–PD-1 therapy. *Sci. Transl. Med*. 9, eaal3604 (2017). **6.** Song, J. et al. Antigen-presenting cancer associated fibroblasts enhance antitumor immunity and predict immunotherapy response. *Nat. Commun*. 16, 2175 (2025). **7.** Voabil, P. An ex vivo tumor fragment platform to dissect response to PD-1 blockade in cancer. *Nat. Med*. https://doi.org/10.1038/s41591-021-01398-3 (2021) doi:10.1038/s41591-021-01398-3. **8.** Ramasubramanian, T. S., et al. A live tumor fragment platform to assess immunotherapy response in core needle biopsies while addressing challenges of tumor heterogeneity. *BioRxiv Prepr Serv Biol* (2025). **9.** Siwczak, F., Hiller, C., Pfannkuche, H. & Schneider, M. R. Culture of vibrating microtome tissue slices as a 3D model in biomedical research. *J. Biol. Eng*. 17, 36 (2023). **10.** Li, Y. et al. Precision vibratome for high-speed ultrathin biotissue cutting and organ-wide imaging. *iScience* 24, 103016 (2021). **11.** Helmlinger, G., Yuan, F., Dellian, M. & Jain, R. K. Interstitial pH and pO2 gradients in solid tumors in vivo: High-resolution measurements reveal a lack of correlation. *Nat. Med*. 3, 177–182 (1997). **12.** Dewyse, L., Reynaert, H. & Van Grunsven, L. A. Best Practices and Progress in Precision-Cut Liver Slice Cultures. Int. *J. Mol. Sci*. 22, 7137 (2021).

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