User Manual

elive™ Edge

Version 1.3

For automated cutting of core needle biopsies into live tumor fragments prior to ex vivo assessment as part of the elive platform

elive™

Table of Contents

The elive platform

The elive platform enables ex vivo profiling in settings of limited tissue

The elive platform enables ex vivo culture of live tumor fragments (LTFs) created from core needle biopsies (CNBs) to assess response to immunotherapy. CNBs are cut into LTFs approximately 300 µm in thickness

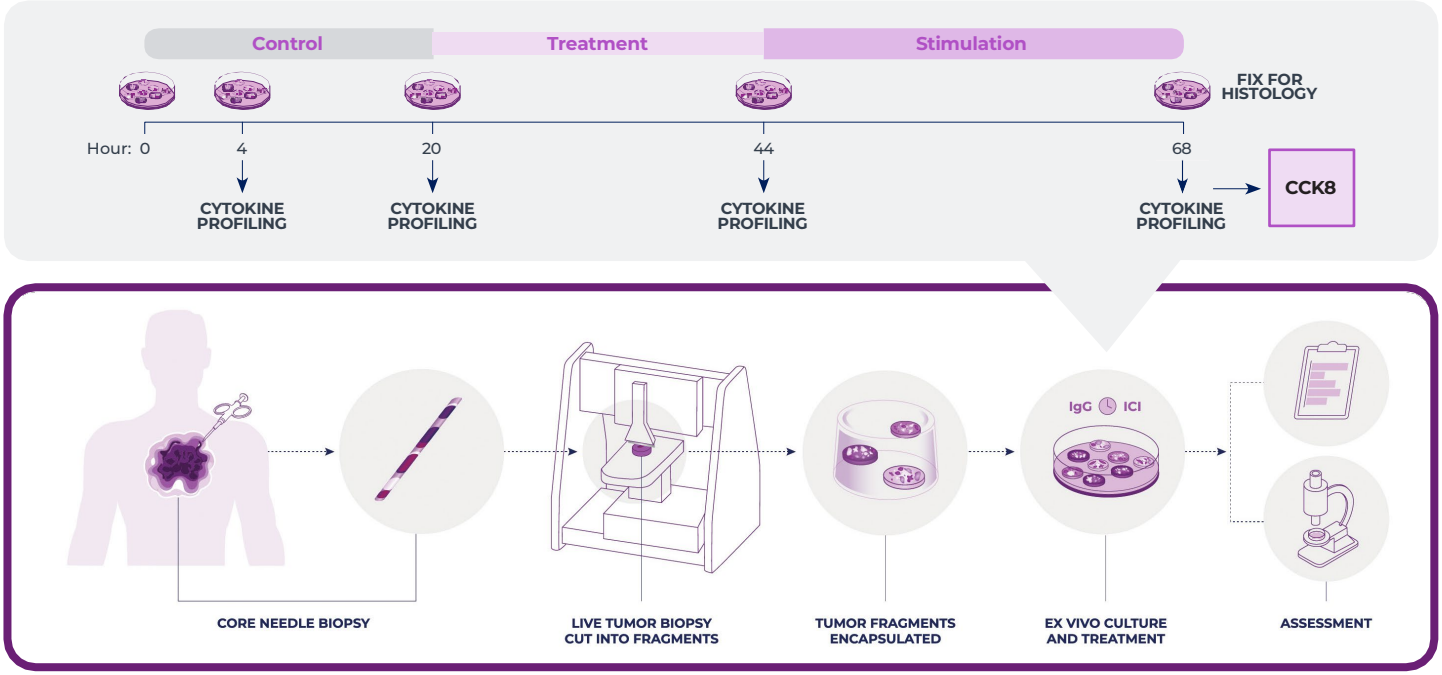


Figure 1. An overview of the Elephas elive platform, highlighting elive Method. LTFs are created by cutting human CNBs on elive Edge. LTFs are encapsulated in elive Gel and treated using elive Method, an approach that applies IgG control (0-20 hours) and ICI (20-44 hours) sequentially to the same tissue in a single well. Response to ICI is assessed by cytokine profiling at the indicated time points.

The elive platform comprises elive Edge, an automated cutting instrument that creates LTFs from CNBs, and elive Gel, a proprietary hydrogel that preserves features of the native tumor microenvironment (TME).

Additionally, the platform incorporates elive Method, a novel sequential treatment strategy that addresses the challenge of intraspecimen heterogeneity in a setting of limited tissue.

Unlike conventional approaches that rely on FFPE tissue, the elive platform profiles live tumor tissue from CNBs, without freezing, allowing a rapid assessment of treatment response. The platform preserves large contiguous areas of TME, which improves the ability to accurately predict response to immunotherapy.

Cytokine profiling is performed longitudinally to assess treatment response. Together, these components enable a novel form of immunotherapy response assessment—live tumor profiling that preserves the native TME and captures functional cytokine responses to treatment.

Related Resources

- elive Gel User Manual
- elive Method User Manual
- Human Tissue Culture Media User Guide

Product Description

elive Edge, an automated cutting instrument, is used to precisely cut clinically relevant tissue form factors, such as CNBs, while preserving large contiguous areas of the native TME for ex vivo experiments. A unique feature of the elive Edge is its ability to cut at an angle. Cutting at an angle balances the need for maximizing the amount of intact TME while also accounting for the difficulty of cutting small, delicate pieces of tissue, such as CNBs, which is an essential component of the elive platform.

Warnings and Precautions

- This product is for research use only.
- The elive Edge instrument must be installed within a Biosafety Cabinet (BSC) by an Elephas representative prior to operation.
- Biosafety: Handle human tissue in accordance with institutional biosafety protocols. Human tissue samples may contain bloodborne pathogens or other transmissible agents. Always follow universal precautions and approved handling procedures and personal protective equipment (PPE) to minimize exposure risk.
- Chemical and media spills: Exercise caution when working with buffers and tissue media. Clean up any spills or splashes immediately according to established safety procedures and notify appropriate laboratory personnel.
- Fixation fumes: Fixation chemicals may emit hazardous fumes; perform fixation steps in a fume hood whenever possible.
- Safety Data Sheets: Review and understand the Safety Data Sheet (SDS) for each hazardous chemical prior to use.
- Sharps safety: Handle scalpels, forceps, and other sharp tools with caution.
- Burn Risk: During agarose preparation, the solution may be hot. Handle containers with care to avoid burns.

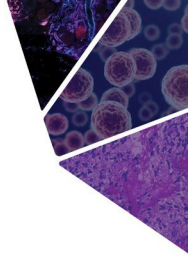
Instrument Operation Hazards

The instrument features a moving blade and moving stages that can present safety risks to operators. The following labels on the instrument indicate safety hazards.

The instrument has been designed, tested, and verified to meet the requirements of:

- IEC 61010-1 Safety requirements for electrical equipment for measurement, control, and laboratory use
- IEC 61326-1 Electrical equipment for measurement, control, and laboratory use - EMC requirements

Hazards	Hazard Sign	Description
Hand Crush Hazard		Moving stages may cause parts of the body to be caught between or drawn into crush points and injured.
Moving Blade Hazard		Moving blades may cut parts of the body causing injury.
Pinch Point Hazard		Moving stages may cause parts of the body to be caught between or drawn into pinch points and injured.
Biological Hazard		Working with tissue should be treated as a biological hazard.



Required Materials and Equipment

Materials

- elive Edge Sample Holder Assembly
- elive Edge Embedding Mold
- elive Edge Blade Assembly
- Petri dish (60mm)
- Agarose, low melt (LM)
- Human tissue culture media, refer to User Guide for more information
- DPBS (Gibco, 14190-144)
- Isopropanol 70% (IPA)
- Broad-spectrum disinfectant
- Kimwipes
- Reverse osmosis (RO) water, or equivalent

Equipment

- elive Edge v1.3
- Biosafety cabinet (BSC)
- Torque screwdriver
- Wecker spatula 5” 2x30mm sterling
- 10cm long angled smooth 1mm tip forceps
- Heat block
- Pipette aid
- Serological pipettes
- Analytical balance
- Microwave
- Vortex
- Incubator
- Refrigerator (4°C)
- Waste aspirator

Instructions

Tissue requirements

- Minimum tissue length to cut on elive Edge is 3 mm regardless of biopsy gauge. Do not cut on the Edge instrument if measured length of the CNB is less than 3 mm.
- The embedding mold can accommodate CNBs up to 25 mm in length. If the total length of the CNB exceeds 25 mm, bisect the tissue using a scalpel or surgical scissors to allow for multiple cuts on elive Edge.

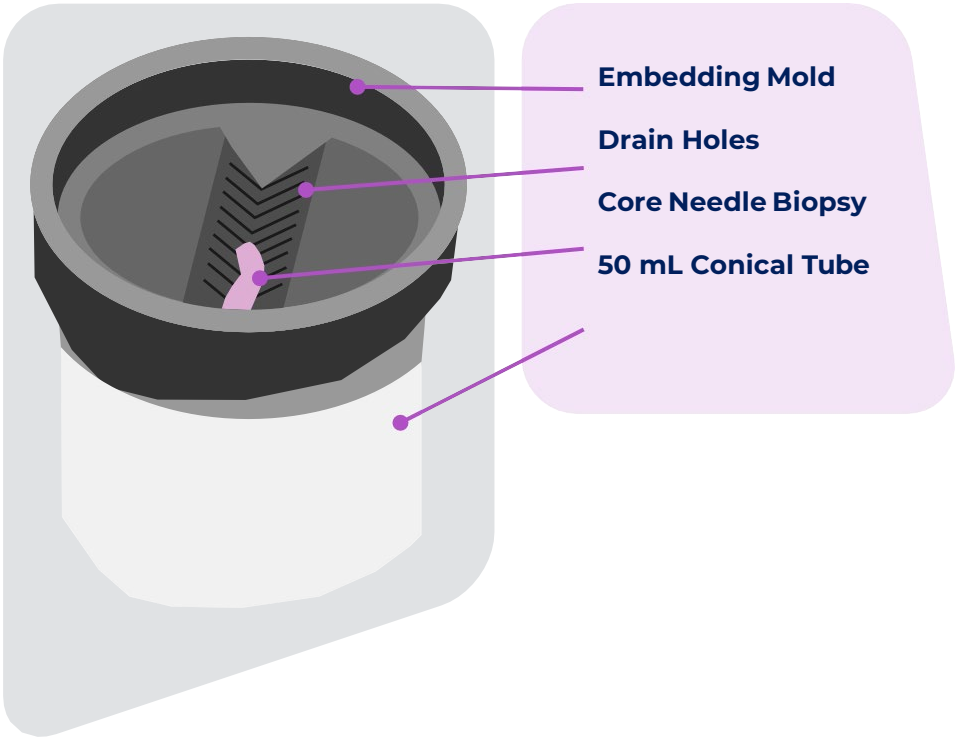
Agarose Preparation

1. To a 50mL conical tube, add 21 mL DPBS using a serological pipette. Weigh and add 0.8 g agarose to the tube and vortex ~10 sec to combine, ensuring no clumps remain.
2. Loosen conical tube cap and place agarose in microwave, maintaining tube in an upright orientation using a heat-safe tube rack.
3. Microwave solution for approximately 10 seconds. Fully tighten tube cap, then vortex solution at highest setting for approximately 10 seconds.
4. Repeat steps 2 and 3 three times, reducing microwave time to 5 seconds on the last repeat. The diluent volume may reduce slightly during boiling. However, if agarose boils out of the conical tube, discard and reprepare.
5. Fully tighten cap and place tube in heat block at 35 to 39 °C. Allow agarose solution to equilibrate on a heat block for at least 15 minutes prior to use.

Sample Preparation

1. Thoroughly clean and disinfect all tools and instruments, and place in BSC. Ensure equipment is free of residue or contamination by following proper disinfection protocols to minimize risk of sample cross contamination. To preserve tissue viability, maintain samples in a tube or dish over wet ice while preparing workstation and between processing steps.
2. Place embedding mold over 50 mL conical tube. Pour the core needle biopsy (CNB) and media into the embedding mold. Media will seep through the drain holes on the bottom of the mold.
    a. If excess media is visible around the sample, gently tap the tube ~3 times against the workstation to break surface tension and allow proper drainage. If the media still does not drain, remove by pipetting.
    b. Discard excess media waste into a biohazard container.
3. Using forceps, position the CNB horizontally along the drain holes and ensure it rests flush along the bottom of the mold. Gently dry any residual media and moisture with a Kimwipe. Avoid contact with the biopsy.

Sample Holder



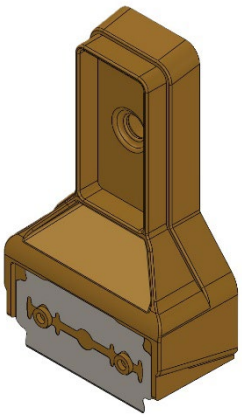
4. Dispense 7.5 mL of 37°C agarose along the ridges of the mold. Firmly press the sample mount into the embedding mold and place on ice for 5 to 30 minutes. Begin instrument setup while the agarose solidifies.

Setup and Cutting

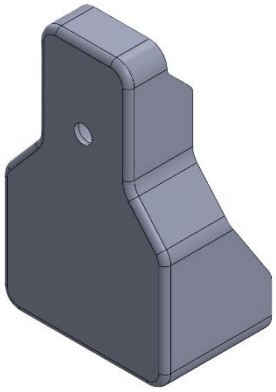
Instrument must be placed in safe state before accessing.

In case of emergency, press the Emergency Stop Button to immediately halt all instrument motion. If the Emergency Stop Button is activated, contact Elephas Technical Support for further guidance

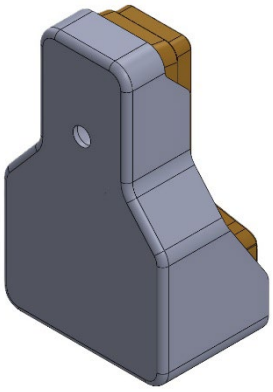
5. Open the elive Edge application and select “Connect” from the home page. Wait until the system successfully connects. If the system fails to connect, refer to Troubleshooting Steps.
6. Once connected, select “Calibrate Stages” and wait for the flexure stage to move to its programmed positions. After calibration is complete, the Main Menu screen will appear. Verify that today’s date is correct. If not, close and reopen the application.
7. Select the appropriate biopsy gauge from the drop-down menu (e.g., 9G, 12–18G or 20G).
8. Select “Load Blade.”
9. Load an elive Edge blade assembly onto the flexure stage blade mount and fasten the assembly screw to 4 in-lbs. Press “Next” to continue.



Blade Holder

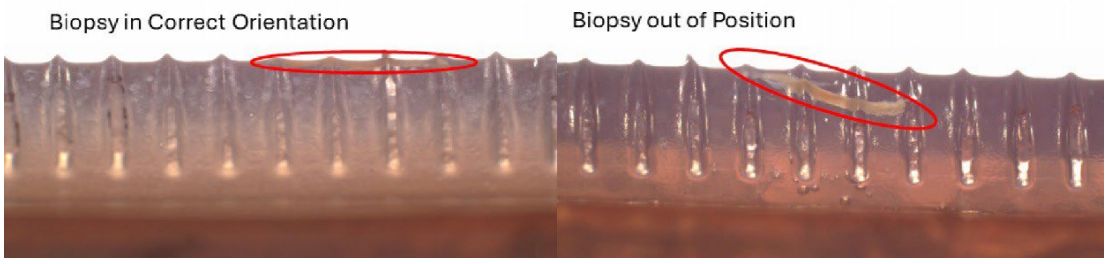


Blade Guard



Blade Holder Assembly

10. Remove the blade guard. Press “Continue” to proceed.
11. Remove sample holder assembly from the ice bath and gently separate the sample holder from the embedding mold.
12. Ensure the biopsy is level at the top of the agarose mold and has not sunk into the agarose mound.



13. If the biopsy rests flush at the top of the agarose mound, proceed with the cutting process.
    a. If the biopsy is misaligned, off-center, or has sunk below the top of the agarose mound, carefully remove it from the agarose mound and re-prepare the sample following the steps in Sample Preparation.
14. Select “Section Biopsy.”
15. Follow the on-screen instructions for sample holder insertion onto the sectioning platform.
16. Select “Continue” once the sample is loaded. A prompt will appear to verify the sectioning blade position.
17. Follow the prompt and confirm the blade and sample holder are mounted properly. There should be ~1 mm between the agarose mound and the blade. If there is contact between the blade and the agarose mound, unload the blade and mount a new one. If the problem persists, check that the agarose did not solidify at an angle. Be sure to firmly and evenly push the sample holder into the embedding mold.
18. Close the sash to the BSC and select “Continue” after verifying the blade position.
19. The instrument will begin sectioning the biopsy sample. Once sectioning starts, periodically monitor the status of the biopsy cutting. If the biopsy is pulled out of the gel, select “Stop” to halt the run and refer to Reprocessing section below.
20. While sectioning is in progress, fill a petri dish with approximately 2 mL of culture media to serve as the collection dish for sectioned LTFs.
21. Once sectioning is complete, remove the sample holder from the sectioning platform and dip the agarose mound containing the sectioned sample into the collection dish.
22. Using non-serrated forceps, carefully remove all tissue LTFs from the agarose mound and transfer them into the collection dish, ensuring that all LTFs are fully submerged. Dispose of the sample holder in a biohazard container.
23. Inspect the sectioning blade for any remaining LTFs. If LTFs are stuck to the blade, carefully remove them using non-serrated forceps and transfer them into the collection dish.
24. End the current cut by selecting “Unload All”. A prompt will appear to add blade guard. Use a torque driver to attach the blade guard and remove the blade assembly from the blade mount and place it in a designated sharps container. Press “Continue” when done to end the protocol.

If the application is halted in any prior steps in response to instrument performance or a technical issue, contact Elephas Technical Support.

Product Specifications

Electrical Requirements	Instrument Power Supply Model: EA1300Q-480 P/N: Zaber PS15S (See Appendix for Marking Label)	Input: 100-240~5.0-2.5A, 50/60 Hz Output: 48V⎓6.5A / 310W Insulation Rating: ≥100 MΩ Safety Ratings: UL, CUL, TUV, CB, CE, FCC, UKCA
Operating Environment	Temperature	18 ℃ - 30 ℃
	Relative Humidity	20% - 80%

Cleaning & Maintenance

After every use, spray a Kimwipe broad-spectrum disinfectant (PREempt or equivalent) and wipe down the instrument. Wait one minute before spraying a Kimwipe with RO water followed by IPA. Refrain from spraying the instrument directly.

Troubleshooting

- If agarose boils over during microwaving, discard and remake the agarose.
- If the CNB floats when agarose is added, carefully remove the CNB with forceps, place it in fresh media, and prepare it again in a new embedding mold.
- If the CNB does not rest flush on top of the agarose mound after the solidification process, restart the sample preparation process.
- If the software does not load properly, verify that the Emergency Stop is not engaged, close out of the software and restart. If the problem persists, contact Elephas Technical Support.
- Verify gauge selection prior to starting the cutting process as an incorrect selection may prevent the blade from fully sectioning the tissue.
- Prior to servicing, unplug the instrument from the power outlet to ensure that the instrument is in a safe state.

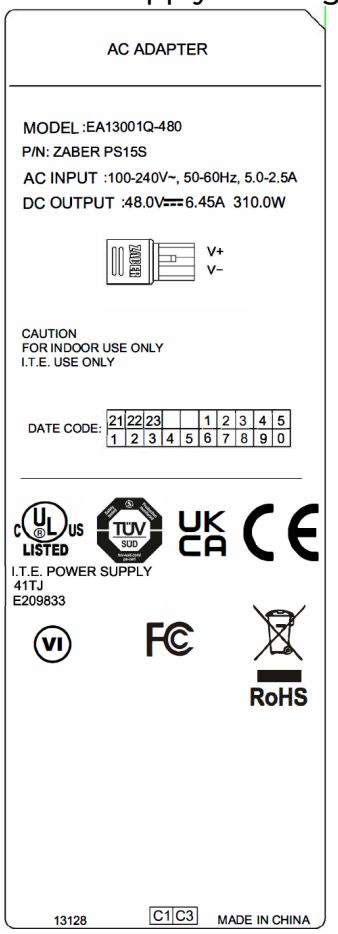
Reprocessing

If the biopsy becomes dislodged or is not successfully cut on the first attempt, user may return to Sample Preparation section and follow steps to re-prepare a new mount and proceed to standard Setup and Cutting.

1. Press “Stop” to halt current run. Follow prompt for returning the sectioning blade to a parked position.
2. Carefully remove the sample holder and retrieve biopsy from the agarose mound and the blade using non-serrated forceps. Be especially mindful when working with exposed blades.
3. Abort the current cut by selecting “Unload All”.
4. If the CNB is still greater than 3 mm in length, return to Sample Preparation and follow the protocol. Remove as much agarose from the tissue as possible prior to sample preparation, taking care to avoid damaging the tissue.

Appendix

1. Power Supply Marking Label:



2. Emergency Stop Button:
   Emergency stop button can be pressed in the event of an emergency or any kind of hazard situation arises from the instrument to the operator. Once pressed, rotate red button clockwise to release the emergency stop and continue operation.

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