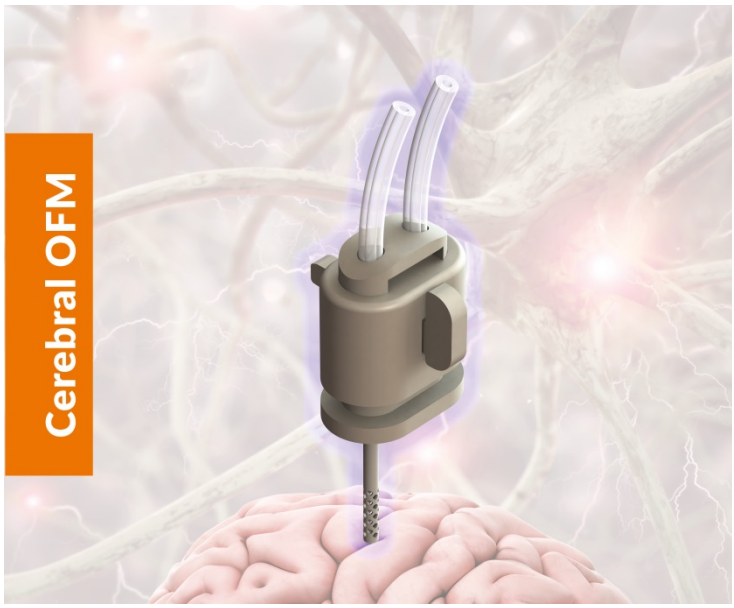
Instructions for Use
–
Cerebral OFM (cOFM) Probe



Product number: cOFM Probe Kit for Brain Tissue (cOFM-P-X-Y)

consisting of:

Guide + Healing Dummy (cOFM-GD-X-Y)
Sampling Insert (cOFM-S-Z)
cOFM-LOCK
All parts can also be ordered individually

Patent number:
EP 2,709,704
US 9,656,018

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1 Overview

READ Instructions for Use before using the cOFM Probe. ALWAYS follow the warnings, cautions, and notes throughout this document. If you have questions regarding the safe or correct use of the cOFM Probe, please contact the American distributor:

BASi (https://www.basinc.com/ask)

U.S. PHONE NUMBER +1-800-845-4246

2 Intended Use

The cOFM Probe is a minimally invasive concentric-type probe for use in brain tissue of laboratory animals, such as mice, rats, dogs, pigs, and primates.

CAUTION

1. **ONLY USE** cOFM Probe on laboratory animals or ex-vivo setups**.**
2. **DO NOT** use on humans! This cOFM Probe has **NOT** been approved for use on humans!
3. **DO NOT** use cOFM Probe on household pets and other non-laboratory animals.

The cOFM Probe provides easy access to the target tissue. The cOFM Probe allows extracting fluid samples from the target tissue enabling to analyze its biochemical conditions. For example the cOFM Probe gives the opportunity to sample substances in the cerebral interstitial fluid of brains with intact blood brain barrier (BBB). Therefore, a physiologically compatible liquid ('perfusate') is passed through the cOFM Probe at a very low flow rate (0.1 - 10µl/min) ('microperfusion').

Due to the open (membrane-free) exchange surface, the perfusate can absorb practically any substances in the surrounding environment. Afterwards, the collected sample fractions of the perfusate can be sent to the laboratory for analysis.

3 Safety Information

3.1 Explanation of Symbols

Symbol	Meaning
	Designates the order number, which also represents the type designation for the cOFM Probe.
	Lot number
	Date of production
	Name and address of manufacturer
	Always observe the Instructions for Use before using the cOFM Probe.
	The cOFM Probe is delivered Gamma irradiated and may only be used once, re-sterilization is not permitted.
	Do not use the cOFM Probe if individual packaging is damaged.
	Store dry.
	Storage temperature must be between 4°C – 40°C.
	Here the irradiation point is attached, which indicates if cOFM Probe was exposed (red = exposed).
	Identifies a warning statement that warns about the possibility of injury, death, or other serious adverse reaction associated with the use or misuse of the device.
	Additional safety instructions must be observed in the Instructions for Use.
	Used cOFM Probe are biohazards and must be disposed accordingly.
	Wear sterile protective gloves while operating cOFM Probe.

3.2 General Warnings and Safety Instructions

WARNING

1. **READ** Instructions for Use prior use.
2. **DO NOT** use on humans! The cOFM Probe has **NOT** been approved for use on humans.
3. **DO NOT** use on household pets or other animals that are not laboratory animals. cOFM Probes are designed **ONLY** for use in laboratory animals!
4. **ALWAYS** wear sterile disposable protective gloves when operating pump and accessories to avoid any contamination or risk of infection.
5. **ONLY** use the cOFM Probe **ONCE**! **DO NOT** reuse, reprocess or sterilize. Reuse leads to the potential risk of serious injury and/or infection, which can result in death.
6. The cOFM Probe is has been sterilized through Gamma Irradiation Processing. **DO NOT** use the cOFM Probe, if the packaging is damaged.
7. **DO NOT** use the cOFM Probe, if the label is missing or illegible.
8. **DO NOT** use the cOFM Probe, if kinked or damaged.
9. **ONLY** use sterile aids for insertion.
10. Stereotactic equipment is recommended for insertion.
11. **ONLY** use sterile, physiologically compatible fluids for perfusion.
12. When using electrical equipment (e.g. micro perfusion pump) in connection with the cOFM Probe, the general electrical safety regulations for the use of electrical equipment must be considered.
13. **ALWAYS** observe animals throughout the application.
14. **KEEP** the cOFM Probe in the packaging until used to prevent mechanical damage and to protect it from light.
15. **STORE** the cOFM Probe under dry and dark conditions. **DO NOT** store the cOFM Probe in a heavily contaminated environment.
16. **STORE** the cOFM Probe between 4°C – 40°C.

4 Directions for Use

4.1 Included Parts of cOFM Probe

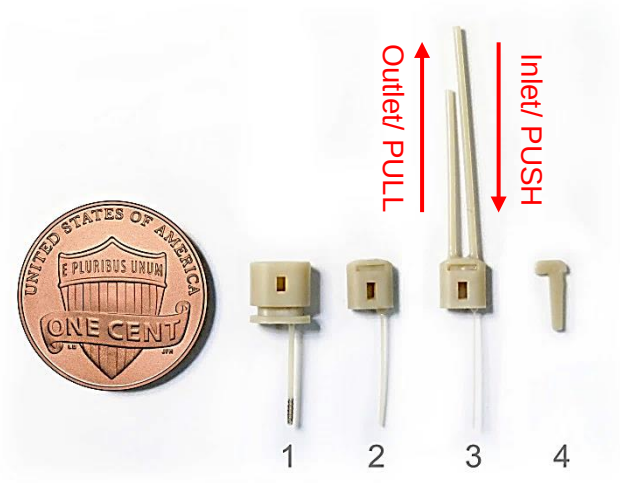

Figure 1: Included parts of cOFM Probe:
(1) Guide, (2) Healing Dummy, (3) Sampling Insert, and (4) Locking Wedge (2x)

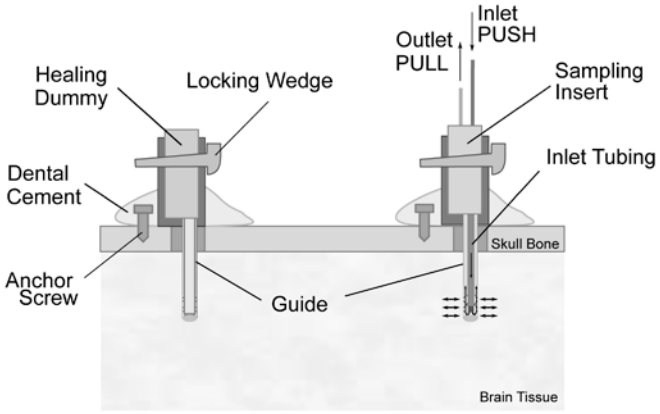

Figure 2: Schemata of implanted cOFM Probe

4.2 Inserting cOFM Probe Into Brain Tissue (Step-by-Step)

1. Guide (1) and Healing Dummy (2) are ready to implant when delivered.
2. Prepare a clean surgical area in order to avoid immune reactions.
3. Prepare the stereotactic apparatus with the anesthesia mask for the appropriate animal size.
4. Prepare the surgical instruments, the eye cream, the shaver, the dental drill and the dental cement within easy reach.
5. Anesthetize the animal with appropriate anesthetic for an anesthesia of 30 to 45min.
6. Fix the animal into the stereotactic apparatus.
7. Shave the fur on the head and disinfect the skin

8. Make a midline incision to expose lambda and bregma.
9. Use the stereotaxic apparatus to identify the desired position of the cOFM Probe and the fixation screws (e.g. 2 for mice and 3 for rats)
10. Drill 3 0.7 mm holes into the skull above the chosen site.
11. Puncture the dura carefully with a needle
12. Fix the cOFM Probe with the appropriate adapter to the stereotaxic apparatus and implant the cOFM guide cannula using the stereotaxic apparatus for exact positioning of depth with a speed of 1mm/min.
13. Insert screws with a screw driver.
14. Place the dental cement around the guide cannula and the fixation screw.
15. When dental cement is cured remove the probe holder from the cOFM Probe.
16. Close the skin above the dental cement and leave the cOFM body point out of the skin.
17. Recover the animal from anesthesia in a warm place.
18. Apply antibiotic (e.g. Cefotaxin) for the first 3 days after surgery.
19. Let the BBB recover for 14 days.

4.3 Connecting cOFM Probe (Step-by-Step)

20. cOFM Probes can be connected as follows:

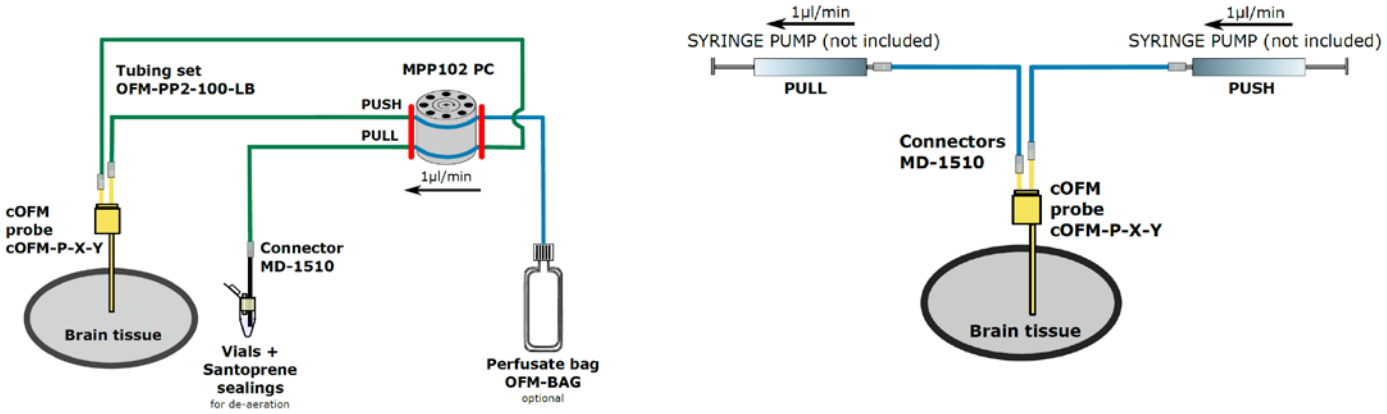

Figure 3a: cOFM Probe connected to MPP10x b:) cOFM Probe connected to syringe pumps (Alternative

21. Connect inflow (PUSH) of Sampling Insert (3) via tubing to the perfusate bag of the MPP10x or PUSH syringe.
22. Connect ouflow (PULL) of Sampling Insert (3) via tubing to fraction collector or PULL syringe.
23. Flush all tubing of the Sampling Insert (3) (e.g. 5µl/min).
24. Replace the Healing Dummy (2) with the Sampling Insert (3). Therefore remove Locking Wedge (4) and Healing Dummy (2) carefully. Pay attention when inserting Sampling Insert (3) into Guide (1). Do not kink the thin PUSH tube. To guarantee correct functionality of cOFM Probe, Sampling Insert (3) must be locked by a new Locking Wedge (4).
25. The connection of the cOFM Probe and the other components is described in detail in the Instructions for Use of the MPP10x pump.
26. Flush the system (e.g. 5µl/min)
27. Perform a run-in phase at sampling flow rate for one hours before starting sampling.

CAUTION

- **ALWAYS** observe Instruction for Use of the Pump MPP10x.
- **ALWAYS** operate cOFM Probe in PUSH/PULL-mode!

28. Apply strain relief to the tubing in a way that unintentional slipping or snagging is avoided.

BIOHAZARD

Used and removed cOFM Probes are biohazards and must be disposed accordingly!

5 Combination with Other Products

The manufacturer recommends using the cOFM Probe with the following products from the manufacturer JOANNEUM RESEARCH Forschungsgesellschaft m.b.H.:

- Microperfusion Pump MPP10x
- OFM Tubing Sets (single-/multi-channel)
- OFM Perfusate Bag
- Flanged Tubing Connector (inner diameter 0.6 to 0.8mm)
- Interconnecting Tubing (outer diameter 0.6 to 0.8mm)

CAUTION

- When using above-listed products with the cOFM Probe, **ALWAYS** observe the Instructions for Use of the respective product!
- Use the cOFM Probe with other manufacturers' products **AT OWN RISK!**