RadioGel® / IsoPet®

Vivos, Inc.

Procedure for Surrogate Hydrogel Yttrium Phosphate Injections

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Review and Approval

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Document Revision History

Revision No.	Date	Description/Rationale
00	7/2/2022	Initial Issuance

1. **Introduction**

The procedures described herein are provided for consideration based on practical experience reported by veterinarians who have used ISOPET™ for the treatment of canine and feline sarcomas. These are in addition to, but do not supersede or replace information provided in the current version of the ISOPET™ product labeling. All warnings, precautions, contraindications, and safety considerations that are delineated in the product labeling should be observed and followed.

2. **Materials**

a. Surrogate tissue (one or more samples)

Fresh (not frozen) chicken breast has been used most commonly for this procedure. Have enough samples on hand to perform multiple injections. A standard ISOPET™ dose can provide up to 50 0.1 ml injections. Plan to administer as few or as many individual injections as needed to gain proficiency. A suggested quantity is up to 10 injections per sample.

b. Warming unit for the chicken breast to reach ~100 ^{o}F internal temperature
c. Magnetic mixer
d. Hydrogel in a serum vial (supplied by Vivos), store at 4 ^{o}C upon receipt (hydrogel is a solution at low temperature and a gel at body temperature)
e. Holder for the yttrium phosphate vial (supplied by Vivos)
f. Non-radioactive YPO_4 particles in a serum vial with stir bar (supplied by Vivos)
g. Serum vial containing erioglaucine blue dye, 10 mg/mL concentration (supplied by Vivos)
h. Syringe shields (supplied by Vivos)
i. 1 cc syringes with 22/25-gauge needles – Luer lock syringes are preferred for radiation safety purposes
j. Ice water bath for the hydrogel
k. Optional – plastic-backed absorbent pads, absorbent cotton or paper wipes, cotton tipped swabs used for radioactive contamination control.

3. **Procedure**

a. Before beginning ensure the chicken breast is at or slightly above internal body temperature.

A convenient method is to place the chicken breast in a zip lock bag (remove as much air as possible to enhance heat transfer) and immerse in a portable cooler filled with hot tap water. Use an instant read thermometer to keep the bath temperature at or slightly above the target temperature and

hold the chicken breast in the bath long enough for the temperature to equilibrate – approximately 15 min.

b. While the surrogate tissue is equilibrating prepare the materials and injection area.

c. Retrieve the hydrogel vial from the refrigerator where it has been stored and place in a cold-water bath (ice plus water) **Do Not Allow the Hydrogel to Freeze.**

d. Place the yttrium phosphate serum vial in the vial holder on top of the magnetic mixer.

e. Turn the mixer on to agitate the yttrium phosphate particles.

f. While mixing, place a vent needle in the septum and cover with gauze

g. Add 0.1 to 0.2 mL of erioglaucine blue dye to the hydrogel yttrium phosphate serum vial. Fill a 5 to 10 mL syringe with the hydrogel and inject into the yttrium phosphate particle vial.

A standard ISOPET™ dose consists of 1 ml of YPO_4 particle suspension with 0.1 ml of blue dye and 4 ml of hydrogel added.

h. Remove the surrogate tissue sample from the temperature-controlled storage.

i. Pat the surface dry and optionally use a marker to lay out a grid of injection points spaced 5 – 8 mm apart.

j. Using a 1 ml syringe withdraw 0.1 to ~0.5 mL of the yttrium phosphate hydrogel mixture.

Typically, a 1 ml syringe with a 25-gauge needle is suitable for both withdrawing and administering ISOPET™. Some users prefer to use a 22-gauge needle for faster loading of the syringe then switch to 25 gauge for injection.

k. A good practice is to invert the syringe to allow air bubbles to rise then move the plunger to eject the air. If this is done after removing the needle from the vial use a sterile pad to catch any droplets exiting the needle.

l. Slowly inject ISOPET™ into the surrogate tissue. 0.1 mL aliquots at ~1 cm depth is recommended for a typical treatment plan. Partially withdraw the needle then hold for ~5 seconds to minimize/avoid backflow along the needle track

m. Watch the blue dye at the point of injection for leakage – If there is leakage, fill a disposable glove with warm water and place on the chicken breast to warm the next area for injection

n. Repeat injections according to the grid pattern until the syringe is emptied. Use additional syringes as needed to complete the injection grid pattern.

An alternative method of administration, especially for larger tumors, is columnar injections either vertically or laterally through the tissue. Typical volume administered is 0.1 ml of ISOPET™ injected per 1 cm of tissue depth. For this

type of administration inject the material continuously while slowly withdrawing the needle. With surrogate tissue limit the amount of ISOPET™ to 0.2 to 0.3 ml per injection for testing purposes.

o. Optional - After injection, hold the tissue at temperature for several minutes to ensure the ISOPET™ has fully gelled. Then use a scalpel to dissect the chicken breast either along the needle track or perpendicular to the track to observe the extent of perfusion.

4. Disposal

a. Unused ISOPET™ may be stored under refrigeration for additional testing. The ISOPET™ components are non-toxic and unused material and injected chicken breasts may be stored or disposed of as normal waste.