**Biokinetics and dosimetry of $^{99m}$Tc-iFAP of healthy male volunteers**

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**Purpose:** Fibroblast Activation Protein inhibitors (iFAP's) are considered promising targets for radionuclide-based approaches for diagnosis of tumors associated with a remodeling of the extracellular matrix. Recently, the National Institute for Nuclear Research of Mexico (ININ) has designed a radiopharmaceutical based on the iFAP, the $^{99m}$Tc-iFAP. This study assessed the quantification of $^{99m}$Tc-iFAP through the conjugate-view method (2D) and the hybrid approach (2D/3D) in four male volunteers.

**Methods:** Anterior and posterior whole-body planar images (at 1, 3, 6 and 24 h, Fig.1A), and SPECT/CT images (6.5 h, Fig.1B) were acquired after $^{99m}$Tc-iFAP administration (740 MBq) in 4 healthy male volunteers. Planar images were corrected for attenuation, scattering and radioactive decay. SPECT/CT images were corrected for attenuation, scattering, partial volume effect and radioactive decay. 2D and SPECT/CT images were quantified with the conjugate-view method and the 3D method, respectively. Correction factors between imaging modalities were calculated to scale the activity obtained from planar imaging, and applied in the quantifications of the 2D method to obtain the volumetric activity quantification.

The fraction of the injected activity of each organ were fitted to three-exponential models and the absorbed doses were obtained using OLINDA/EXM following an individualized approach.

**Results:** Figure 1A shows the whole-body planar images of volunteer 1 acquired at different times. Figure 1B depicts the reconstructed SPECT/CT image of the same volunteer acquired at 6.5 h. The 2D method overestimated the activity quantification of the liver ( $0.58 \pm 0.06$) and kidneys ($0.35 \pm 0.05$).

Table 1 summarizes the mean biokinetic models and the average number of nuclear transformations that occurred in the source organs of the healthy male volunteers, following the planar and hybrid methodology. Table 2 shows the average equivalent and effective doses of $^{99m}$Tc-iFAP, calculated from the four volunteers for each methodology.

**Conclusions:** This is the first report in which $^{99m}$Tc-iFAP was assessed in healthy Mexican male volunteers. The effective dose calculated by both methods is at the level recommended for diagnostic studies (<10 mSv), these results suggest that the use of $^{99m}$Tc-iFAP is safe to start its assessment in cancer patients.

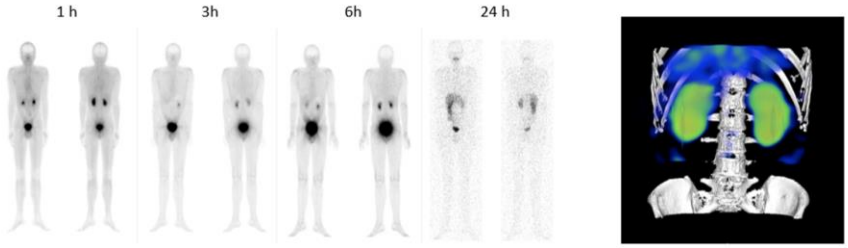


**Figure 1:** A) Planar images of the volunteer 1 after the administration of $^{99m}$Tc-iFAP (740 MBq). Anterior and posterior whole-body at 1,3,6 and 24 h after radiotracer administration B) SPECT/CT of volunteer 1 after 6.5 h of $^{99m}$Tc-iFAP administration.

**Table 1.** Biokinetic models of $^{99m}$Tc-iFAP calculated from four healthy male volunteers by a planar and hybrid methodology.

**2D Method**

| Organ | Biokinetic models | $N = \int_0^\infty A(t)_{ROI}dt$ (MBqh/MBq) (mean ± SD) |
|---|---|---|
| Urinary bladder | $A(t)_{ROI} = 2.76e^{-0.247t} + 9.61e^{-0.3t} + 0.891e^{-0.247t}$ $R^2 = 0.99$ | 0.53 ± 0.13 |
| Kidneys | $A(t)_{ROI} = 4.67e^{-1.395t} + 6.87e^{-0.8t} + 3.14e^{-0.202t}$ $R^2 = 1$ | 0.26 ± 0.05 |
| Heart | $A(t)_{ROI} = 0.745e^{-0.942t} + 1.64e^{-0.697t} + 1.10e^{-0.275t}$ $R^2 = 1$ | 0.07 ± 0.02 |
| Liver | $A(t)_{ROI} = 1.66e^{-0.432t} + 4.20e^{-0.465t} + 1.24e^{-0.181t}$ $R^2 = 1$ | 0.20 ± 0.02 |
| Remainder of the body | $A(t)_{ROI} = 45.1e^{-0.558t} + 56.2e^{-0.399t} + 4.45e^{-0.169t}$ $R^2 = 1$ | 2.48 ± 0.26 |

**Hybrid method**

| Organ | Biokinetic models | $N = \int_0^\infty A(t)_{VOI}dt$ (MBqh/MBq) (mean ± SD) |
|---|---|---|
| Urinary bladder | $A(t)_{VOI} = 2.76e^{-0.247t} + 9.61e^{-0.3t} + 0.891e^{-0.247t}$ $R^2 = 0.99$ | 0.53 ± 0.13 |
| Kidneys | $A(t)_{VOI} = 1.03e^{-1.102t} + 2.42e^{-0.889t} + 1.07e^{-0.205t}$ $R^2 = 1$ | 0.09 ± 0.02 |
| Heart | $A(t)_{VOI} = 0.745e^{-0.942t} + 1.64e^{-0.697t} + 1.10e^{-0.275t}$ $R^2 = 1$ | 0.07 ± 0.02 |
| Liver | $A(t)_{VOI} = 0.629e^{-0.418t} + 2.47e^{-0.465t} + 0.654e^{-0.182t}$ $R^2 = 1$ | 0.11 ± 0.02 |
| Remainder of the body | $A(t)_{VOI} = 48.8e^{-0.612t} + 63.2e^{-0.394t} + 6.01e^{-0.17t}$ $R^2 = 1$ | 2.96 ± 0.49 |

**Table 2.** Average equivalent and effective doses (mSv/MBq) of $^{99m}$Tc-iFAP, calculated from four healthy volunteers.

| Target Organ | 2D Method Equivalent doses (mean ± SD) | | | Hybrid Method Equivalent doses (mean ± SD) | | |
|---|---|---|---|---|---|---|
| Adrenals | 3.58E-05 | ± | 3.81E-06 | 3.12E-05 | ± | 3.31E-06 |
| Brain | 1.21E-05 | ± | 6.00E-07 | 1.44E-05 | ± | 1.49E-06 |
| Breasts | 1.33E-04 | ± | 8.34E-06 | 1.50E-04 | ± | 1.50E-05 |
| Gallbladder Wall | 3.61E-05 | ± | 2.93E-06 | 3.24E-05 | ± | 3.32E-06 |
| LLI Wall | 3.58E-04 | ± | 4.76E-05 | 3.91E-04 | ± | 5.56E-05 |
| Small Intestine | 1.50E-05 | ± | 1.38E-06 | 1.58E-05 | ± | 1.78E-06 |
| Stomach Wall | 2.38E-04 | ± | 1.77E-05 | 2.46E-04 | ± | 2.46E-05 |
| ULI Wall | 1.41E-05 | ± | 1.17E-06 | 1.47E-05 | ± | 1.59E-06 |
| Heart Wall | 4.11E-05 | ± | 5.60E-06 | 4.28E-05 | ± | 5.93E-06 |
| Kidneys | 1.80E-04 | ± | 4.25E-05 | 7.42E-05 | ± | 2.07E-05 |
| Liver | 2.40E-04 | ± | 3.04E-05 | 1.65E-04 | ± | 2.87E-05 |
| Lungs | 2.01E-04 | ± | 1.26E-05 | 2.18E-04 | ± | 2.21E-05 |
| Muscle | 2.07E-05 | ± | 1.70E-06 | 2.25E-05 | ± | 2.43E-06 |
| Pancreas | 3.07E-05 | ± | 2.71E-06 | 2.89E-05 | ± | 2.93E-06 |
| Red Marrow | 2.13E-04 | ± | 2.25E-05 | 2.26E-04 | ± | 2.62E-05 |
| Osteogenic Cells | 4.60E-05 | ± | 6.53E-06 | 5.21E-05 | ± | 7.30E-06 |
| Skin | 1.06E-05 | ± | 7.06E-07 | 1.19E-05 | ± | 1.19E-06 |
| Spleen | 3.04E-05 | ± | 3.38E-06 | 2.78E-05 | ± | 2.94E-06 |
| Testes | 1.64E-04 | ± | 2.04E-05 | 1.83E-04 | ± | 2.51E-05 |
| Thymus | 2.22E-05 | ± | 1.70E-06 | 2.52E-05 | ± | 2.57E-06 |
| Thyroid | 7.79E-05 | ± | 3.89E-06 | 9.21E-05 | ± | 9.31E-06 |
| Urinary Bladder Wall | 1.25E-03 | ± | 3.15E-04 | 1.27E-03 | ± | 3.18E-04 |
| Prostate | 1.57E-04 | ± | 2.98E-05 | 1.66E-04 | ± | 3.13E-05 |
| Effective Dose (mSv/MBq) | 3.53E-03 | ± | 5.08E-04 | 3.50E-03 | ± | 5.39E-04 |