FIRST EXAMPLE OF A ^{99m}Tc-LABELED-FLUOROQUINOLONE IN A TUMOR ANIMAL MODEL

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Introduction: Fluoroquinolone (FQ) antibiotics are well-known bacterial DNA gyrase inhibitors and ^{99m}Tc-labeled fluoroquinolones have been applied as infection imaging agents. It is known that structural modifications can convert FQs to mammalian topoisomerase inhibitors. In our previous work, we synthesized a FQ-complex, rhenium-tricarbonyl-enrofloxacin-imidazole (Re-erx/im) which exhibited increased inhibition of Topo IIα compared to erx.[1] We aim at assessing ^{99m}Tc-labeled enrofloxacin-imidazole (^{99m}Tc-erx/im) in different animal model groups for its potential as an infection- or tumor-targeted imaging agent.

Methodology: Two groups of BALB/c mice with intramuscular oedema were used, the first with bacterial infection by Escherichia coli (group A), the second with aseptic inflammation induced by turpentine (group B). A third group of BALB/c mice (group C) bearing subcutaneously syngeneic murine CT26 tumors was also used. 99mTc-erx/im was injected intravenously and the mice were euthanized at 1h and 2h p.i.. The radioactivity of the infected and inflamed muscle vs this of the normal muscle was measured in groups A and B respectively, as well as the radioactivity of the tumor in group C.

Figure 1. % ID/g in E.coli infected mice

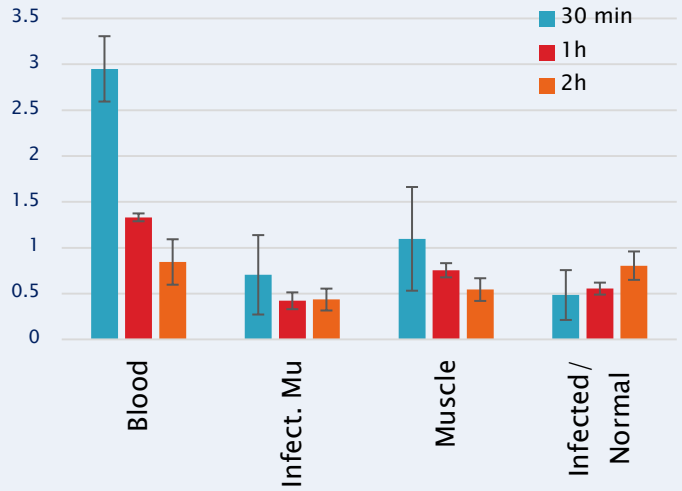
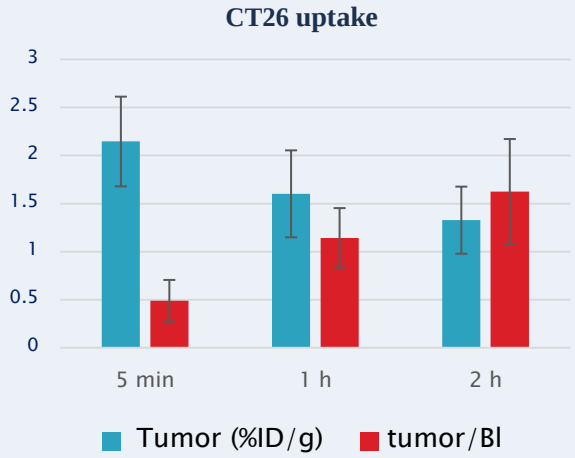
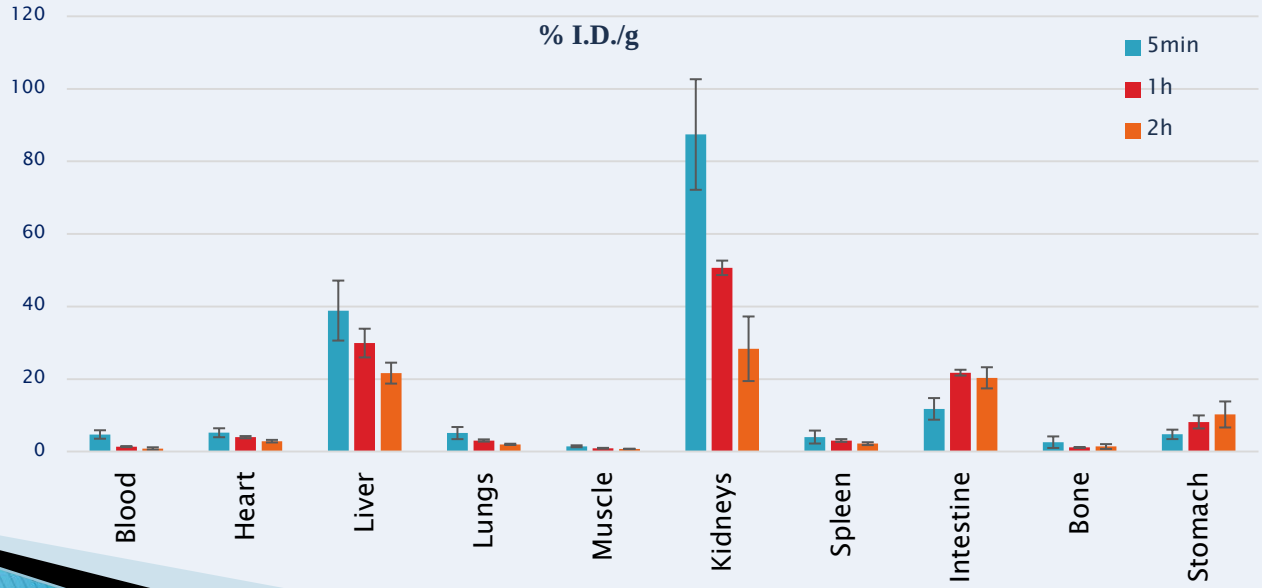


Figure 3. % I.D./g CT26 tumor uptake and tumor/Blood ratio



Α/Α ΖΩΟΥ	ΔΙΑΣΤΑΣΕΙΣ ΌΓΚΟΥ (mm)
1	6 x 6.5
2	7 x 4
3	2 x1 , 2 x 3, 4 x 4.5
4	8.x 5.5
5	7 x 5
6	4 x 3, 6 x 4
7	3 x 4
8	7 x 6.5
9	3 x 9, 3 x 2
10	5.5 x 7.5

Figure 2. % I.D./g of 99mTc-tracer in BALB/c mice



Discussion: The results of the biodistribution show fast blood clearance and excretion both via the renal and hepatobiliary route. No significant accumulation in the infectious foci was observed and the infected-to-normal muscle ratio is <1 at all time points. Low CT26 accumulation was observed, which exhibited an increasing tumor/blood ratio overtime.

Conclusions: New design will be required to obtain an infection-specific 99mTc-fluoroquinolone tracer. The observed CT26 tumor uptake is promising and further studies with 99mTc-labeled modified fluoroquinolones with higher affinity for Topo IIα are currently underway.