delayed images were obtained after 24 hours if pyelocaliceal dilation was present. RTF was calculated using both 3-hour and 24-hour images, preferably using semi-automatic regions of interest. The T-Student test was utilized for statistical analysis, considering a difference of ≤ 3% between the two values as not significantly justifying the additional 24-hour image. **Results:** A total of 1,205 consecutive 99mTc-DMSA scans from February 2019 to December 2023 were evaluated. Group 1 comprised 662 patients, with 62 undergoing additional 24-hour imaging, while Group 2 consisted of 543 patients, with 43 undergoing 24-hour imaging. The mean value of the difference between the 3h and 24h images is 1.95% ± 1.83% and median 2 (0 - 6) for Group 1, and 2.40% ± 2.08% and median 2 (0 - 8) for Group 2. Statistical analysis demonstrated equivalence between RTF quantifications obtained at 3-hour and 24-hour imaging for Group 1 $p < 0.0001$, 95% confidence interval (1.45 - 2.42). However, for Group 2, quantifications at 3-hour and 24-hour imaging were not necessarily equivalent $p = 0.0714$, 95% confidence interval (1.76 - 3.05). **Conclusion:** Additional 24-hour imaging with 99mTc-DMSA in patients under 12 years of age with pyelocaliceal dilation does not appear to impact RTF compared to 3-hour images. However, for older patients, 24-hour imaging is necessary for greater accuracy in RTF determination. Further investigations are warranted to better understand factors influencing RTF calculation, guiding the indication for additional 24-hour imaging.

**Keywords:** DMSA, Hydronephrosis, Nuclear medicine, RTF.

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## ACCESSING THE PHARMACOKINETICS OF MAGNETIC NANOPARTICLES IN CIRRHOSIS-ASSOCIATED HEPATOCARCINOGENESIS BY ORDINARY DIFFERENTIAL EQUATION MODELING AND AC BIOSUSCEPTOMETRY

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**Introduction/Justification:** Magnetic nanoparticles (MNPs) have been explored as a new potential theranostic agent, and several studies have devoted significant efforts to employ MNPs in biomedicine, including their applications as imaging contrast agents in alternating current biosusceptometry (ACB). In this field, the novelty of multichannel alternating current biosusceptometry (MC-ACB) devices allow the generation of real-time magnetic images of processes of biodistribution of MNPs in essays with animal models, including experiments focused on liver diseases. **Objectives:** This study refers to the in vivo biodistribution of MNPs detected by the multichannel ACB system, aimed at how the pharmacokinetics of MNPs is affected in the case of hepatocellular carcinoma. This evaluation has already been presented in a previous paper in terms of experimental results, but not in terms of pharmacokinetic modeling. **Materials and Methods:** In order to quantitatively describe how this disease may alter the biodistribution of MNPs, two different groups of animals are addressed here: a control group of healthy animals (SAL) and a group of animals with hepatocellular carcinoma (DEN/TAA). The MC-ACB system was used to simultaneously record the transit of MNPs in the heart and their accumulation in the liver. Pharmacokinetic rates of change of MNPs are reported here by proceeding with population parameter estimation for two groups of animals: cancer (DEN/TAA) and control (SAL). They refer to the change of MNPs from heart to liver (k1), from liver to heart (k2), and as the irreversible uptake of MNPs by Kupffer cells within a liver subcompartment (k3). All animal experiments were previously approved and performed according to the protocol 7571041120 by the Ethics Committee on Animal Use of the State University of São Paulo (IBB/UNESP). **Results:** Notably, both k2 and k3 were found to differ between groups, but not k1, consistent with the fact that MNP liver pharmacokinetics are expected to be affected by the chemically induced cirrhosis-associated hepatocarcinogenesis of the DEN/TAA group. The fact that k2 and k3 are higher for the DEN/TAA group is related to earlier MNP liver saturation in cirrhosis due to higher blood volume, and cirrhosis-associated hepatocarcinogenesis is revealed to affect the biodistribution of magnetic nanoparticles. **Conclusion:** The modeling approach proposed in the research provides a powerful tool to quantitatively describe the biodistribution of magnetic nanoparticles in healthy and cirrhotic rats, allowing the estimation of pharmacokinetic rate parameters related to the distribution of magnetic nanoparticles. The introduced modeling robustly describes the concentration of nanoparticles in compartments over time, which may assist in the development of targeted drug delivery strategies. Finally, this study highlights the relevance of mathematical modeling for understanding complex phenomena such as nanoparticle interactions with living systems, particularly in the development of effective theranostic applications.

**Keywords:** Cirrhosis-associated hepatocarcinogenesis, Magnetic nanoparticles, Ordinary differential equations, Parameter estimation, Pharmacokinetic modeling.

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