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Development of ^{99M}tc-Labeling Protocol for Hydrogel-Based Microspheres

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1. INTRODUCTION

Hydrogel microspheres are biocompatible, hydrophilic and non-resorbable polymeric systems which are increasingly used as biomedical carriers to target and deliver diagnostic and therapeutic agents.[1] These microspheres usually consist of a swollen network of hydrophilic polymer chain with water content exceeding 95%, which guarantees elasticity, compressibility and stability. The conjugated groups are responsible for the carrier feature of the particles.[2]

The aim of this study was to develop an easy and effective protocol for radiolabeling LifePearl® microspheres with ^{99m}Tc-pertechnetate. LifePearl® is produced from polyethylene glycol chain and additional sulfonate groups which enable the loading of the beads with chemotherapeutic agents.[3] This drug delivery system has been applied in FDA-approved manner as a trans-arterial chemoembolization (TACE) agent for the treatment of unresectable hepatocellular carcinoma.

2. MATERIALS AND METHODS

For radiolabeling procedure LifePearl® microspheres (Terumo European Interventional Systems, Leuven, Belgium; size range 100 ± 25 um) were used. The labeling process started with the chemical reduction of ^{99m}Tc-pertechnetate ($^{99m}TcO_4^-$; *Synthesis route No1*). For this purpose, freshly made special 'Reducing agent' was composed from 0.1% stannous-chloride, 0.2% ascorbic acid and concentrated hydrochloric acid for pH adjustment (pH 4-5). Next, the microspheres were incubated with the radioactive solution (30-50 MBq; mixing ratio varied between 1:5 to 5:1) at room temperature for various incubation time (10 min – 1 h). Following the auto-sedimentation of the gel-like ^{99m}Tc-microspheres the supernatant was discarded and the labeling efficiency, the retention factors (R_f) of the particles were determined by using instant thin layer chromatography (ITLC). For quality control (QC), instant thin-layer chromatography paper impregnated with silica gel (ITLC-SG; Agilent Technologies, Santa Clara, US) was used as stationary phase and 0.9% Saline was applied as solvent (mobile phase). The reading out of chromatographic paper was made by miniGITA scanning device (Elysia-raytest, Straubenhardt,

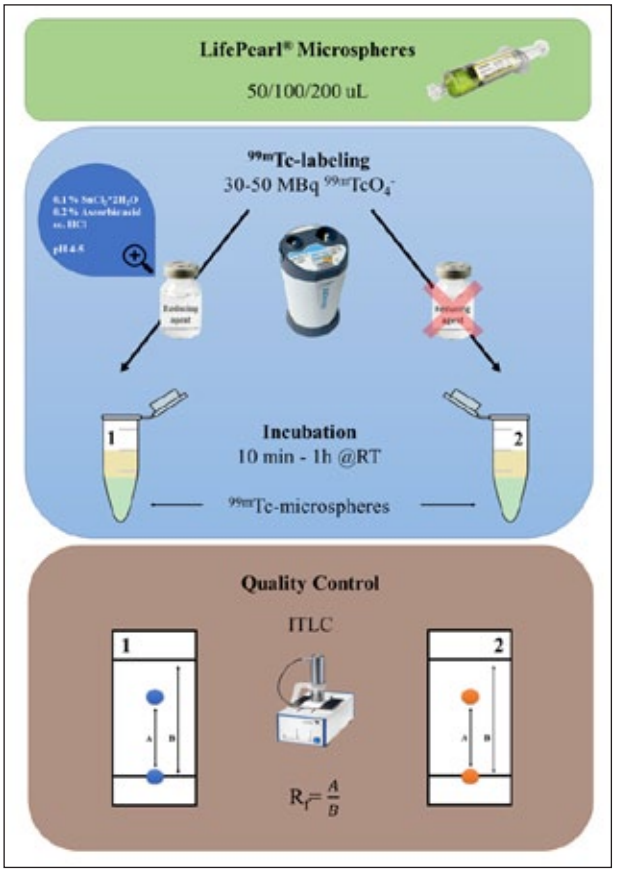

Figure 1 *The synthesis scheme of ^{99m}Tc-labeled microspheres. (1) Labeling with 'Reducing-agent'. (2) Labeling without 'Reducing-agent'.*

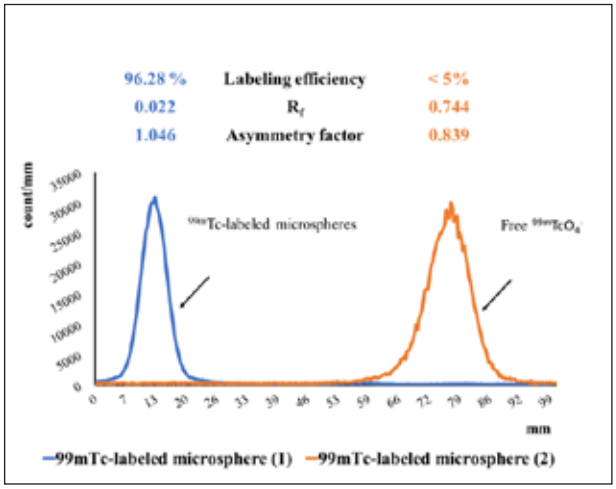

Figure 2 *The ITLC chromatograms of the sample*

Germany). The whole labeling procedure and quality control process were repeated without the application of 'Reducing agent' as negative control (*Synthesis route No2*) (see ***Figure 1***).

3. RESULTS

The radiolabeling efficiency exceeds 95 % by *Synthesis route No1* (blue curve) and remained constant for several hours. It was independent from the applied microsphere concentration. In contrast, labeling with the unreduced form of ^{99m}Tc-pertechnetate (*Synthesis route No2; orange curve*), as a negative control, resulted negligible labeling efficiency (less than 5%) (***Figure 2***).

4. CONCLUSION

The developed labeling protocol of LifePearl® microspheres is an easily applicable method to monitor the biodistribution of particles applied in oncologic therapy and to determine critical biodistribution of TACE agents.

5. ACKNOWLEDGEMENTS

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