Supplementary materials

Linking in vivo imaging to therapeutic outcome with ^{131}I, ^{177}Lu, ^{188}Re nanoparticles

Yulia Finogenova [1,2]*, Alexey Lipengolts [1,2,3]*, Olga Klementyeva [1], Kristina Shpakova [1,2], Vsevolod Skribitsky [1,2,3], and Elena Grigorieva [1,2]

[1] N.N. Blokhin National Medical Research Center of Oncology, Moscow 115522, Russia;
o.klementeva@ronc.ru (O.K.); shpakova.k.e@gmail.com (K.S.); skvseva@yandex.ru (V.S.); grig-elen11@mail.ru (E.G.)
[2] Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Moscow 119991, Russia
[3] Institute for Physics and Engineering in Biomedicine, National Research Nuclear University "MEPhI", Moscow 115409, Russia
* Correspondence: ju.finogenova@ronc.ru (Y.F.); lipengolts@ronc.ru (A.L.)

The table summarizes all experimental studies reviewed in this work that include both diagnostic imaging (SPECT or PET) and radionuclide therapy performed on the same tumor model with the same route of administration. Color coding indicates the degree of correlation between imaging findings and therapeutic outcomes:

- Dark green: strong correlation.
- Light green: correlation is observable.
- White: insufficient data to establish correlation.
- Light blue: combination therapy; SPECT/PET correlates with the effect of isolated nanoradiopharmaceutical.

This assessment is inherently subjective and reflects the authors' interpretation of the available evidence.

References are numbered according to the main text.

Table S1. Studies with ^{131}I-labeled nanoparticles. Abbreviations: IV (intravenous injection), IT (intratumoral injection), PTT (photothermal therapy), PDT (photodynamic therapy), SDT (sonodynamic therapy).

Radionuclide (therapy)	Nanoparticle platform	Targeting agents	Tumor model (therapy)	Administration	Imaging	SPECT (or PET) findings	Combination therapy	Therapeutic outcome	Reference
^{131}I	^{131}I-G5·NHAc-HPAO-PEG-FA (PAMAM dendrimer)	Folic acid	C6 rat glioma, subcutaneous	IV	Clinical SPECT (^{131}I), 2 min–24 h	6–24 h: brighter tumor signal for targeted vs non-targeted dendrimers	—	Tumor growth: 8.78-fold (targeted), 17.16-fold (non-targeted), 18.51-fold ($Na^{131}I$), 26.65-fold (saline). Survival: 25% after 38 d (targeted) vs 0% after 31 d (non-targeted)	J. Zhu et al., 2015 [65]
^{131}I	^{131}I-G5.NHAc-HPAO-(PEG-CTX)-(mPEG) (PAMAM dendrimer)	Chlorotoxin	C6 rat glioma, subcutaneous	IV	Clinical SPECT (^{131}I), 5 min–24 h	6–24 h: higher tumor signal intensity for targeted vs non-targeted dendrimers	—	Tumor growth: 7.27-fold (targeted), 10.67-fold (non-targeted), 13.07-fold ($Na^{131}I$), 16.7-fold (saline). Survival: 25% after 40 d (targeted) vs 25% after 35 d (non-targeted)	L. Zhao et al., 2015 [66]
^{131}I	^{131}I-G5.NHAc-HPAO-(PEG-BmK CT)-(mPEG) (PAMAM dendrimer)	BmK CT (chlorotoxin-like peptide)	C6 rat glioma, subcutaneous	IV	Clinical SPECT (^{131}I), 5 min–24 h	1–24 h: higher tumor radioactivity for targeted vs non-targeted dendrimers	—	Tumor growth inhibition: targeted > non-targeted > $Na^{131}I$ > saline. Survival: 50% after 39 d (targeted) vs 50% after 32 d (non-targeted)	Y. Cheng et al., 2016 [67]
^{131}I	^{131}I-Au PENPs-CTX (PEI-entrapped gold nanoparticles)	Chlorotoxin	C6 rat glioma, subcutaneous	IV	Clinical SPECT (^{131}I), 0.5–16 h	Peak at 8 h: tumor signal 2.4-fold higher for targeted nanoparticles vs non-targeted	—	Tumor growth: 9.7-fold (targeted), 18.2-fold (non-targeted), 19.6-fold (saline). Survival: 25% at 48 d (targeted) vs 25% at 34 d (non-targeted)	L. Zhao et al., 2019 [68]
^{131}I	BmK CT-Au PENPs-^{131}I (PEI-entrapped gold nanoparticles)	BmK CT (chlorotoxin-like peptide)	C6 rat glioma, subcutaneous	IV	Clinical SPECT (^{131}I), 0.5–16 h	Peak at 8 h: tumor signal 2.11-fold higher for targeted nanoparticles vs non-targeted	—	Tumor growth: 7.36-fold (targeted), 19.88-fold (non-targeted), 21.91-fold (saline). Survival: 25% after 45 d (targeted) vs 0% at 34 d in all other groups	N. Sun et al., 2019 [69]

^{131}I	^{131}I@PEI-AuNPs (PEI-coated gold nanoparticles)	—	C6 rat glioma, subcutaneous	IT	Clinical SPECT (^{131}I), 1 min–24 h	^{131}I@PEI-AuNPs: high thyroid uptake, but 20% remained in the tumor at 24 h post-injection. Free Na^{131}I: <2%	—	Tumor growth: 5.04-fold (^{131}I@PEI-AuNPs), 12.36 (Na^{131}I), 12.33-fold (saline). Survival: 20% at 31 d (^{131}I@PEI-AuNPs) vs 0% at 16 d (saline)	M. Zhu et al., 2024 [39]
^{131}I	PNS.NHAc-HPAO(^{131}I)-PS (polyphosphazene nanospheres)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IT	Clinical SPECT (^{131}I), 5 min–12 h	Nanospheres: 81% of initial tumor signal retained at 12 h post-injection. Branched PEI: 33%, free Na^{131}I: 13%	—	Tumor growth: 1.42-fold (^{131}I-nanospheres), 6.69-fold (branched ^{131}I-PEI), 7.60 (Na^{131}I), 8.10-fold (saline). Survival: 80% at 35 d (^{131}I-nanospheres), 20% at 35 d (branched ^{131}I-PEI), 0% by 30 d (saline)	W. Zhu et al., 2019 [38]
^{131}I	^{131}I-AuNPs-TAT (gold nanoparticles)	TAT (nuclear targeting)	HCT116 human colon cancer, subcutaneous	IT	SPECT/CT (^{131}I), 2 h–168 h	^{131}I-AuNPs-TAT: 20% of initial tumor signal retained at 48 h post-injection; non-targeted ^{131}I-AuNPs: 20% at 24 h	internal radio--immunity therapy (without external immune agents)	Tumor growh inhibition: 79.95% (^{131}I-AuNPs-TAT), 68.98% (^{131}I-AuNPs), 44.74% (free ^{131}I-TAT). Survival: 6/7 at 58 d vs 0% at 34 d in DMEM control group	W. Su et al., 2020 [71]
^{131}I	^{131}I-PS (PEG-PIC polymersomes)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{125}I), 0–192 h + CT (iodine)	Tumor peak at 48 h (17.45 %ID/g); CT density: 66→256 HU at 48 h; no thyroid signal	—	Significantly inhibited tumor growth; survival: 32 d vs 14 d for non-radioactive control	J. Cao et al., 2019 [44]
^{131}I	^{131}I-HSP-PEG (hyperbranched semiconducting polymer nanoparticles)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{99m}Tc) 0.5–24 h for tumor accumulation; SPECT/CT (^{125}I) 1–72 h for metabolism	^{99m}Tc-HSP-PEG: high tumor uptake. ^{125}I-HSP-PEG: liver and spleen retention at 72 h, high kidney and bladder signal — urine excretion	DMXAA administered separately	Tumor growth inhibition: 50% (^{131}I-HSP-PEG), 80% (^{131}I-HSP-PEG + DMXAA)	X. Yi et al., 2018 [45]

^{131}I	^{131}I-RGD-BSA-PCL (albumin +polycaprolactone nanoparticles)	RGD	NCI-H460 human lung cancer (NSCLC), subcutaneous	IT	SPECT/CT (^{131}I), day 1–21	High tumor signal for targeted and non-targeted nanoparticles; weak — for Na^{131}I. At 21 d targeted > non-targeted	—	Both ^{131}I-BSA-PCL (non-targeted) and ^{131}I-RGD-BSA-PCL (targeted) delayed tumor progression vs controls	H. Ming et al., 2017 [37]
^{131}I	^{131}I-HSA-ICG (albumin-indocyanine green nanoparticles)	—	ARO (human anaplastic thyroid carcinoma), subcutaneous	IT	SPECT/CT (^{131}I), 0 h–7 d + NIR fluorescence (ICG) + infrared thermography	^{131}I-HSA-ICG: remained at the tumor site for 4–6 d. Free Na^{131}I: spread to the liver and other organs within 1 h	PTT	Combination therapy (^{131}I-HSA-ICG+laser): significant tumor volume reduction. ^{131}I-HSA-ICG, free Na^{131}I: partial inhibition; HSA-ICG+laser: temporary inhibition with recurrence	X. Zhang et al., 2022 [92]
^{131}I	^{131}I-ZGCs-ZnPcC4 (zinc gallate nanoparticles + photosensitizer ZnPcC4)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IT	SPECT/CT (^{131}I), 1 h–7 d	^{131}I-ZGCs-ZnPcC4: remained in the tumor for 7 d; free Na^{131}I: ~1 h	PDT (without external light)	^{131}I-ZGC-ZnPcC4: tumor size unchanged within 10 d. Free Na^{131}I: no effect	Q. Wang et al., 2020 [99]
^{131}I	rSPNs (radioactive semiconducting polymer nanoparticles)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	Clinical SPECT (^{131}I), 3–36 h + NIR fluorescence + infrared thermography	^{131}I-rSPNs: detectable from 12 h; peak at 24 h	PTT + PDT	Combination therapy (^{131}I-rSPNs+laser): 81.8% tumor inhibition efficacy, which is 1.5-fold higher vs ^{131}I-rSPNs only, 1.3-fold higher vs SPNs+laser. Lung metastases: ~1 nodule (^{131}I-rSPNs+laser), which is 13.3-fold lower vs PBS control, ≥4.0-fold lower vs other treatment groups	N. Yu et al., 2022 [98]

^{131}I	^{131}I-AN@D/IX (polydopamine-modified gold nanostar + protoporphyrin IX)	—	BxPC-3 human pancreatic cancer, subcutaneous	IT	SPECT/CT (^{99m}Tc), 0.5–48 h	^{131}I-AN@D/IX stable intratumor accumulation within 36 h; free Na^{131}I: no signal at the tumor, high at the spleen and thyroid at 2 h	SDT + PTT	Triple therapy: complete tumor regression in 2/3 mice; dual therapies: significant inhibition but no eradication; ^{131}I-AN@D/IX only: partial inhibition	J. An et al., 2023 [100]
^{131}I	^{131}I-TMP@D (polydopamine-coated PLGA nanoplatform + MnTTP + tirapazamine)	—	BxPC-3 human pancreatic cancer, subcutaneous	IT	SPECT/CT (^{131}I) 0–24 h + MRI	^{131}I-TMP@D: gradual decrease of tumor signal for 24 h; minimal thyroid uptake, gradually increasing after 3 h; free Na^{131}I: no signal at the tumor, high at the thyroid at 3 h	SDT + chemotherapy (tirapazamine)	Combination therapy: (^{131}I-TMP@D+US): tumor growth inhibition 97.2%, 1/3 complete eradication. Monotherapy (^{131}I-TMP@D and TMP@D+US): remarkable inhibition. Free ^{131}I: rapid tumor growth	J. An et al., 2025 [101]
^{131}I	^{131}I-PDA-PEG/DOX (polydopamine nanoparticles + doxorubicin)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{99m}Tc) 0.5–6 h	Tumor uptake after 2 h post-injection	chemotherapy (doxorubicin)	Combination therapy (^{131}I-PDA-PEG/DOX): greatly inhibited tumor growth; 100% survival at 4 weeks. Monotherapy (PDA-PEG/DOX or ^{131}I-PDA-PEG): partial tumor growth inhibition. Free DOX + free ^{131}I: unsatisfactory effect	X. Zhong et al., 2015 [85]
^{131}I	^{131}I-Pd-PEG (palladium nanosheet)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{125}I), 20 min–48 h + photoacoustic imaging + infrared thermography + PET/CT (^{18}F-FDG) for therapeutic efficacy monitoring	Clear tumor visualization at 24–48 h, almost zero background in normal organs at 48 h	PTT	Combination therapy (^{131}I-Pd-PEG+laser): significantly inhibited tumor growth, confirmed by ^{18}F-FDG PET/CT. Monotherapy (^{131}I-Pd-PEG or Pd-PEG+laser): delayed tumor growth. Free ^{131}I: no effect	M. Chen et al., 2018 [46]

^{131}I	^{131}I-FDP-Pds (fluorinated palladium nanosheet)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{125}I), 0.5–48 h; SPECT/CT (^{99m}Tc) 0.5–32 h; + photoacoustic imaging + MRI (^{19}F / Gd) + infrared thermography + PET/CT (^{18}F-FDG) for therapeutic efficacy monitoring	^{125}I-FDP-Pds: higher tumor uptake than other organs at 32–48 h (high tumor/normal ratio). ^{99m}Tc-FDP-Pds: tumor + liver uptake (high background). Na^{99m}TcO4, ^{99m}Tc-FDP, Na^{125}I: no tumor uptake	PTT	Combination therapy (^{131}I-FDP-Pds+laser) and PTT (FDP-Pds+laser): superior inhibition, no recurrence for 2 months, confirmed by ^{18}F-FDG PET/CT. Radionuclide therapy (^{131}I-FDP-Pds): significant inhibition. Controls (including free Na^{131}I): uncontrolled growth	Z. Guo et al., 2018 [47]
^{131}I	PMNs-II-813 (melanin-based organic nanoparticles; Mn^{2+})	PSMA-SH	LNCaP human prostate cancer, subcutaneous	IV	PET/CT (^{89}Zr), 2–48 h; PET/MRI (^{89}Zr / Mn^{2+}) 2–168 h for therapeutic efficacy monitoring + photoacoustic imaging + infrared thermography	Tumor uptake: 3.62% ID/g at 2 h, 7.73% ID/g at 24 h, 6.20 % ID/g at 48 h post-injection. Tumor/blood 5.23, tumor/muscle 5.93, tumor/liver 0.93 at 48 h post-injection	PTT	Combination therapy (^{131}I-PMNs-II-813+laser): relative tumor increment rate 2.0% at day 20 (best effect). Radionuclide therapy (^{131}I-PMNs-II-813): 33.2%; PTT (PMNs-II+laser): 38.7%; free ^{131}I: 68.8% at day 20	L. Xia et al., 2021 [52]

Table S2. Studies with ^{177}Lu-labeled nanoparticles. Abbreviations: IV (intravenous injection), IT (intratumoral injection), PTT (photothermal therapy), PDT (photodynamic therapy).

Radio-nuclide (therapy)	Nanoparticle platform	Targeting agents	Tumor model (therapy)	Admin-istration	Imaging	SPECT (or PET) findings	Combina-tion therapy	Therapeutic outcome	Reference
^{177}Lu	^{177}Lu-DOTA-αMSH-PEG-Cy5-C' dots (silica-based hybrid nanoplatform — Cornell prime dots)	αMSH cyclic peptide (melano-cortin-1 receptor, MC1-R)	M21 human melanoma	IV	SPECT/CT (^{177}Lu), 24 h post-injection	Specific tumor uptake; blocked by excess non-radioactive NDP peptide, confirming MC1-R-mediated selectivity	—	Reduced tumor growth. Survival: 58 d (targeted, 0.5 mCi), 43 d (targeted, 1.0 mCi — radiotoxicity); 33 d (non-targeted, 0.5 mCi), 60 d (non-targeted, 1.0 mCi); 27 d (PBS control)	X. Zhang et al., 2020 [64]
^{177}Lu	^{177}Lu-LCP (lipid-calcium-phosphate nanoparticles)	Anisamide (sigma receptor ligand)	UMUC3 human bladder cancer + NIH/3T3 fibroblasts (stroma-rich model), subcutaneous	IV	SPECT/CT (^{177}Lu), 24 h post-injection + Cerenkov luminescence imaging	^{177}Lu-LCP: tumor, liver, and spleen accumulation at 24 h. Free $^{177}LuCl_3$: bone and kidney accumulation, no tumor uptake	—	Sustained and significant tumor growth inhibition compared to free $^{177}LuCl_3$ and nonradioactive ^{175}Lu-LCP control	A. Satterlee et al., 2015 [29]
^{177}Lu	^{177}Lu-DOTA-PEG-CPNs (covalent polymer nanoparticles)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV, IT	SPECT/CT (^{177}Lu), 6–48 h	Intravenous: tumor uptake observed at 24 h, more remarkable at 48 h. Intratumoral: long retention, no whole-body leakage	—	Intravenous: growth delay of ~15 d, median survival 32 d (vs 17 d in control group). Intratumoral: 50% of mice cured, no tumor recurrence within 90 d. Free ^{177}Lu: no effect	X. Chen et al., 2024 [24]
^{177}Lu	^{177}Lu-T-AuNP (PEGylated gold nanoparticles)	Panitumumab (EGFR)	MDA-MB-468 human breast cancer, subcutaneous	IT	SPECT/CT (^{177}Lu), 1–48 h	SPECT signal mostly confined to tumor at 1 h; decreased and more homogeneous at 48 h; similar for targeted and non-targeted. SPECT data also used for tumor dosimetry (voxel-based Monte Carlo modeling)	—	Tumor growth index: 0.3 (targeted), 0.8 (non-targeted), 11.1 (saline). Survival: 100% at 120 d (both) vs 75 d (saline). Complete regression: 3/6 (targeted) vs 1/6 (non-targeted)	S. Yook et al., 2016 [70]

^{177}Lu	^{177}Lu-EuDPA/SiO_2-NH_2 (europium dipicolinate-doped mesoporous silica nanoparticles)	—	HT-29 human colorectal adenocarcinoma, subcutaneous	IT	SPECT/CT (^{177}Lu), 2–48 h	Visible tumor accumulation 2–48 h, little diffusion from injection site	—	Significant inhibition of tumor growth vs non-radioactive control	R. Viana et al., 2020 [26]
^{177}Lu	^{177}Lu-MIL-101(Fe)/PEG-FA (metal-organic framework)	Folic acid	U87MG human glioblastoma, subcutaneous	IT	SPECT/CT (^{177}Lu), 12–48 h + NIR fluorescence	Intratumoral injection: tumor retention with no radioactivity release within 48 h	—	Dose-dependent tumor growth inhibition (1.20, 2.78, 5.55 MBq); free $^{177}LuCl_3$ — limited inhibition. Median survival: 24 d (1.20 MBq), 26 d (2.78 MBq), 32 d (5.55 MBq) vs 18 d (saline)	R. Liang et al., 2023 [27]
^{177}Lu	^{177}Lu-nanostar (polymeric organic nanoplatform)	—	CT26 murine colon carcinoma, subcutaneous	IV	PET (^{89}Zr), 3 days post-injection +MRI	High uptake and clear delineation of CT26 tumor	—	Survival (median): 35 d (7.4 MBq), 24 d (3.7 MBq), 17 d (1.5 MBq), 14 d (non-radioactive control). Tumor growth considerably impaired with increasing dose	J. Goos et al., 2020 [51]
^{177}Lu	^{177}Lu-PCN-PEG (Zr-porphyrin metal-organic framework)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{99m}Tc), 1–24 h + NIR fluorescence	Tumor signal enhanced during 24 h post injection	—	Significant tumor growth inhibition and prolonged survival compared to free ^{177}Lu and non-radioactive controls	Y. Tao et al., 2021 [48]
^{177}Lu	^{177}Lu@AuNCs (glutathione-coated gold nanoclusters)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV, IT	SPECT/CT (^{99m}Tc), 1–24 h; SPECT/CT (^{177}Lu), 1–24 h	^{99m}Tc@AuNCs, ^{177}Lu@AuNCs (intratumoral): longer tumor retention (up to 24 h) vs free ^{99m}Tc and ^{177}Lu. ^{99m}Tc@Au NCs (intravenous): effective tumor accumulation	immunotherapy (anti-PD-L1, administered separately)	Both (!) ^{177}Lu@AuNCs and ^{99m}Tc@AuNCs (intravenous, intratumoral): significantly suppression of tumor growth. ^{177}Lu@AuNCs intratumorally —almost completely suppressed. Free ^{99m}Tc^{177}Lu: no inhibition effect	P. Pei et al., 2021 [49]
^{177}Lu	^{177}Lu-DOTA-DN(PTX)-BN (PAMAM dendrimer)	bombesin (GRPR)	T47D human breast ductal carcinoma, subcutaneous	IT	SPECT/CT (^{177}Lu), 1.5–120 h (1 mouse)	Tumor retention for 120 h	chemotherapy (paclitaxel)	Tumor size reduced by 15.6% at day 5 (1 mouse)	B.Gibbens-Bandala et al., 2019 [83]

^{177}Lu	^{177}Lu-SPN-GIP (semiconducting polymer nanoparticles)	GIP (glucose-dependent insulinotropic polypeptide)	CFPAC-1 human pancreatic ductal adenocarcinoma, subcutaneous	IT	SPECT/CT (^{177}Lu), 0.5–96 h + infrared thermography	Strong tumor signal for 4 days. Free $^{177}LuCl_3$: diffused whole-body signal within 1-day, excretion at day 2	PTT	Combination therapy (^{177}Lu-SPN-GIP+laser): tumor growth inhibition within 21-day observation. Monotherapy (^{177}Lu-SPN-GIP or SPN-GIP+laser): suppression with recurrence. Free $^{177}LuCl_3$: slight suppression	X. Shi et al., 2021 [89]
^{177}Lu	^{177}Lu-PNPs (polymeric nanoparticles)	—	MTCQ-1 oral squamous cell carcinoma, subcutaneous	IV	SPECT/CT (^{177}Lu), 2 and 24 h post-injection + NIR-II fluorescence + infrared thermography	Tumor-to-muscle ratio 3.2 (with PTT) vs 1.3 (without PTT)	PTT	Combination therapy (^{177}Lu-PNP+laser): most apparent tumor retardation and prolonged survival. Monotherapy (^{177}Lu-PNP or PNPs+laser): initial antitumoral effects with regrowth within 10 d	H. Hsieh et al., 2025 [90]
^{177}Lu	^{177}Lu-PPNs, 10 nm (porphyrin-PEG nanocomplexes)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	PET/CT (^{64}Cu), 0.5–72 h; gamma camera imaging (^{177}Lu), 2–14 days + NIR fluorescence	Tumor uptake: 12.5 %ID/g at 24 h, 15.6 %ID/g at 72 h. Tumor/muscle ratio 5.2 at 24 h, 16.6 at 72 h	PDT	Combination therapy (^{177}Lu-PPNs+laser): tumor growth completely inhibited for 14 days. Monotherapy (^{177}Lu-PPNs or PPNs+laser): slight/moderate effect. Free ^{177}Lu: rapid tumor growth	B. Yu et al., 2018 [94]
^{177}Lu	^{177}Lu-GCP-NPs (pH-sensitive glycol chitosan-based nanoparticles)	—	4T1 murine mammary adenocarcinoma, subcutaneous	IV	SPECT/CT (^{99m}Tc), 1–24 h + NIR fluorescence	Strong tumor signal, 8.1-fold higher than for non-pH-sensitive ^{99m}Tc-GCOP-NPs at 8 h	PDT	Combination therapy (^{177}Lu-GCP-NPs+laser): tumor growth inhibition 95.5% — completely suppressed. Monotherapy (^{177}Lu-GCP-NPs or GCP-NPs+laser): moderate effect. Free ^{177}Lu: no effect	Y. Zhang et al., 2022 [95]

Table S3. Studies with ^{188}Re-labeled nanoparticles. Abbreviations: IV (intravenous injection), IT (intratumoral injection), PTT (photothermal therapy), 5-FU (5-fluorouracil), EBRT (external beam radiotherapy).

Radio-nuclide (therapy)	Nanoparticle platform	Targeting agents	Tumor model (therapy)	Admin-istration	Imaging	SPECT (or PET) findings	Combina-tion therapy	Therapeutic outcome	Reference
^{188}Re	^{188}Re-liposomes (liposomes loaded with ^{188}Re-BMEDA)	—	C26 murine colon carci-noma, perito-neal carcino-matosis	IV	SPECT/CT (^{188}Re), 1–72 h	Slow blood clearance, high activity in the abdominal cavity before 24 h. High uptake in ascites, in the tumor, liver, and feces	—	Tumor burden: decrease of 63.4% (vs 9.1% in 5-FU group). Ascites: decrease of 83.3% (vs 44.9% in 5-FU group). Median survival: 32.8 d vs 26.7 (5-FU) and 24.3 (saline)	C.-C. Tsai et al., 2011 [77]
^{188}Re	^{188}Re-liposomes (liposomes loaded with ^{188}Re-BMEDA)	—	LS-174T hu-man colon adenocarci-noma, subcu-taneous	IV	SPECT/CT (^{188}Re), 1–72 h	Tumor SUV: 1.21 (1 h), 9.81 (24 h — peak), 5.87 (48 h), 4.2 (72 h). Liver, spleen accumulation	—	Tumor volume (day 26): 143 mm^3 vs 480 mm^3 (5-FU) and 920 mm^3 (saline). Median survival: 58.5 d vs 48.25 d (5-FU) and 43.63 d (saline)	C.-W. Hsu et al., 2012 [32]
^{188}Re	^{188}Re-liposomes (liposomes loaded with ^{188}Re-BMEDA)	—	4T1 murine mammary ad-enocarcinoma, orthotopic (mammary fat pad)	IV	planar gamma imaging (^{188}Re), 1–24 h; SPECT/CT (^{188}Re), 1–24 h	SPECT: significant tumor accumulation at 24 h. Planar imaging: tumor uptake ~4.59% ID/g at 24 h	—	Small tumor model (50 mm^3): mean growth index 0.49 vs 0 (100% complete regression) in Lipo-DOX group; median sur-vival 28 d vs 59 d (Lipo-DOX) and 23 d (saline). Large tumor model (300 mm^3): mean growth index 0.486 vs 0.062 in Lipo-DOX group, median sur-vival 23 d vs 41 d (Lipo-DOX) and 17 d (saline)	C.-M. Liu et al., 2012 [76]
^{188}Re	^{188}Re-liposomes (liposomes loaded with ^{188}Re-BMEDA)	—	NCI-H292 human non-small cell lung cancer, orthotopic	IV	SPECT/CT (^{188}Re), 1–48 h + SPECT/CT (^{123}I-FIAU) for tumor model validation + bioluminescence imaging for moni-toring therapeutic efficacy	No apparent ^{188}Re signal detected in the orthotopic lung tumor	—	Tumor viability suppressed by ^{188}Re-liposomes, but not by ^{188}Re-BMEDA (assessed by bioluminescence imaging). Median survival: 40 d (^{188}Re-liposomes) vs 26 d (^{188}Re-BMEDA)	L.-T. Lin et al., 2014 [79]

^{188}Re	^{188}Re-liposomes (liposomes loaded with ^{188}Re-BMEDA)	—	FaDu human hypopharyngeal squamous cell carcinoma (HNSCC), orthotopic (buccal cavity)	IV	SPECT/CT (^{188}Re), 4–48 h + SPECT/CT (^{123}I-FIAU) for tumor model validation + Cerenkov luminescence imaging + bioluminescence imaging for monitoring therapeutic efficacy	Apparent accumulation of ^{188}Re-liposome in the lower oral cavity after 24 h, signal reduced after 48 h	—	Tumor growth: suppressed by ^{188}Re-liposome at 12–21 d vs ^{188}Re-BMEDA; regrowth after day 21 (assessed by bioluminescence imaging). Survival: improved in ^{188}Re-liposome group vs ^{188}Re-BMEDA group	L.-T. Lin et al., 2016 [78]
^{188}Re	^{188}Re-liposomes (liposomes loaded with ^{188}Re-BMEDA)	—	BE-3 human esophageal adenocarcinoma, subcutaneous	IV	SPECT/CT (^{188}Re), 1–24 h	Tumor uptake was present in BE-3-bearing mice	EBRT	Tumor growth inhibition rate: 25% (^{188}Re-liposomes), 30% (EBRT), 53% (combination therapy). Three-fold increase delay: 8.3 d (^{188}Re-liposomes), 8.3 d (external radiotherapy), 12.4 d (combination therapy). Additive effect of combination therapy	C.-H. Chang et al., 2015 [102]
^{188}Re	^{188}Re-DXR-liposome (liposomes loaded with ^{188}Re-BMEDA and doxorubicin)	—	C26 murine colon carcinoma, subcutaneous	IV	SPECT/CT (^{188}Re), 1–72 h	Tumor SUV: 1.09 (1 h), 2.97 (4 h), 4.70 (24 h — peak), 2.67 (48 h), 2.07 (72 h). ^{188}Re-BMEDA: no tumor uptake	chemotherapy (doxorubicin)	Mean growth index: 0.048 (^{188}Re-DXR-liposome) vs 0.134 (^{188}Re-liposome) and 0.413 (Lipo-Dox). Median survival: 74 d (^{188}Re-DXR-liposome) vs 60 d (^{188}Re-liposome), 38 d (Lipo-Dox) and 31 d (saline). Synergistic effect. Complete regression: 2/8 at 120 d only in ^{188}Re-DXR-liposome group	Y.-J. Chang et al., 2010 [34]
^{188}Re	^{188}Re-Dox micelles (PEG-PCL polymeric micelles loaded with doxorubicin)	—	BNL/Luc murine hepatocellular carcinoma, orthotopic	IV	SPECT/CT (^{188}Re), 1–48 h + bioluminescence imaging for monitoring therapeutic efficacy	Radioactivity accumulated in the liver and tumor at 1, 4, 24, and 48 h	chemotherapy (doxorubicin)	Tumor growth inhibition: 84.8% (^{188}Re-Dox micelles), 42.0% ($^{188}ReO_4$), 60.7% (Dox-micelles). Survival rate: 80% (^{188}Re-Dox micelles) at day 31 vs 0% in all other groups by day 31	Y.-H. Shih et al., 2015 [80]

^{188}Re	^{188}Re-Au NRs (PEGylated gold nanorods)	—	B16F10 murine melanoma, subcutaneous	IT	SPECT/CT (^{99m}Tc) 1–3 d + infrared thermography	Tumor retention for 3 days	PTT + chemo-therapy (paclitaxel, adminis-tered sepa-rately)	Triple therapy: most significant tumor growth inhibition. Chemotherapy and chemother-apy+PTT: poor inhibition. ^{188}Re-AuNRs and ^{188}Re-AuNRs+laser: increased inhibition. Survival rate: 75% after 25 days (triple therapy) vs 0% by day 25 in other groups	O. Peltek et al., 2023 [50]
^{188}Re	$^{188}ReO_x$-HSA NPs (rhenium oxide nanopar-ticles encapsulated in human serum albumin)	—	B16F10 murine melanoma, subcutaneous	IT	SPECT/CT (^{188}Re) 1–48 h + CT + infrared thermography	Tumor retention for 48 h with minimal leakage and negligible uptake in healthy organs	PTT	Combination therapy ($^{188}ReO_x$-HSA NPs 1.85 MBq + laser two or three times): tumor growth arrested. PTT only, $^{188}ReO_x$-HSA NPs only (0.5 MBq or 0.9 MBq): moderate inhibi-tion. $^{188}ReO_x$-HSA NPs only (2.78 MBq or 3.7 MBq): significantly decreased tumor volume, but radiotoxicity effect	S. Ghosh et al., 2025 [28]