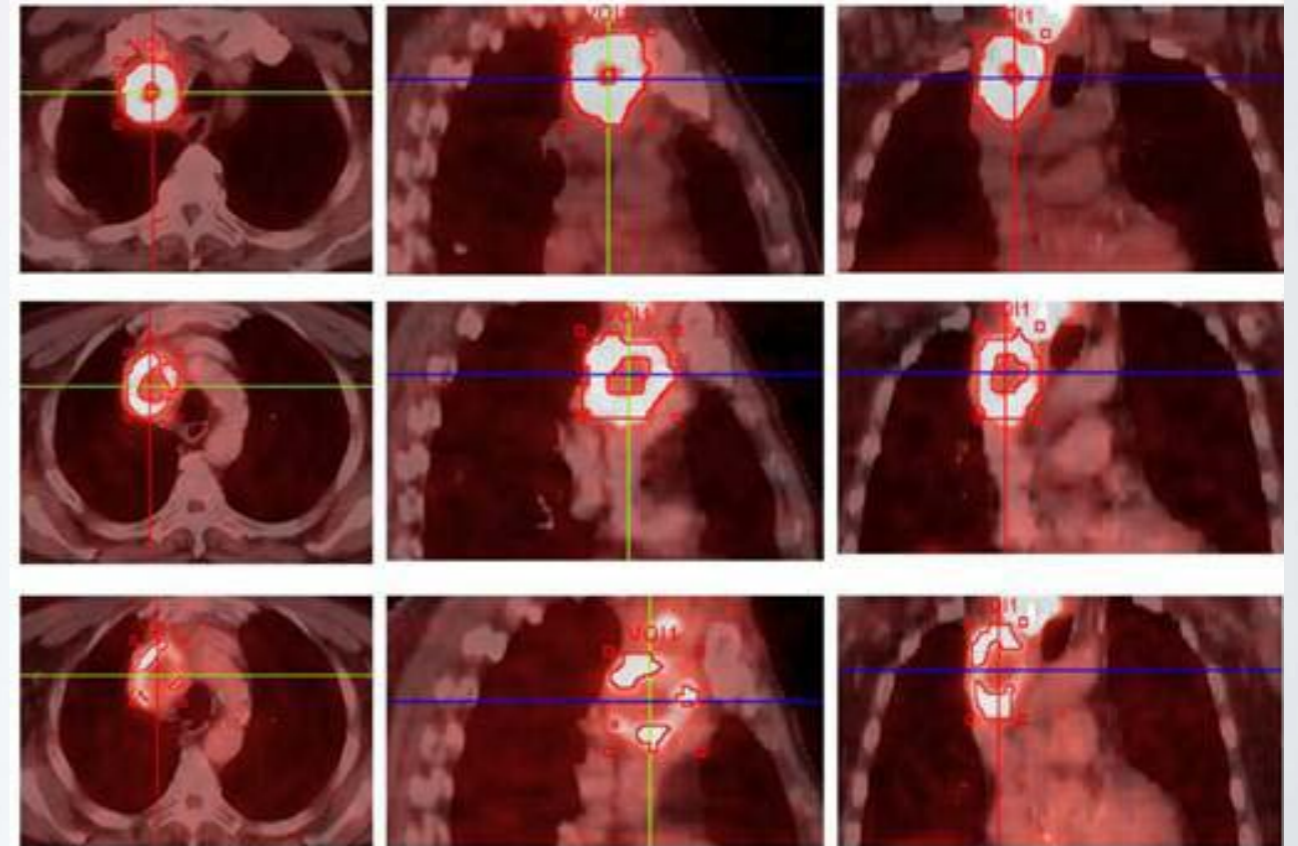
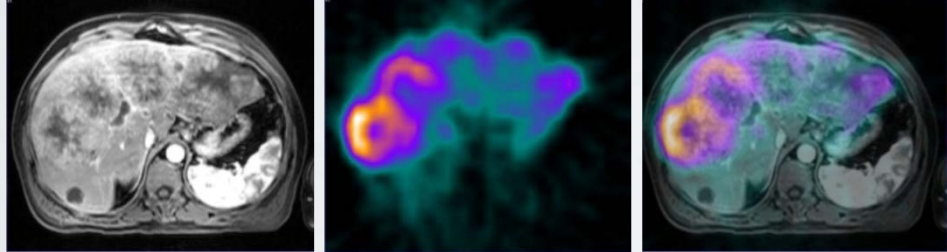


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Therapeutic Radionuclides in Nuclear Medicine: Current and Future Prospects



Key words:

Therapeutic radionuclide

Targeted radionuclide therapy

Radioimmunotherapy

Molecular targeting

Theranostics

This paper reviews the characteristics and clinical applications of the commonly available therapeutic radionuclides, as well as the problems and issues involved in translating novel radionuclides into clinical therapies.



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- 1. Introduction**
- 2. Clinical requirements and choice of radionuclide for therapy**
- 3. Selected therapeutic radionuclides and their clinical applications**
- 4. Molecular targeting radionuclide therapy (Radioimmunotherapy)**
- 5. Current issues and future prospects of therapeutic radionuclides**

Table 1. Physical characteristics of commonly available therapeutic radionuclides

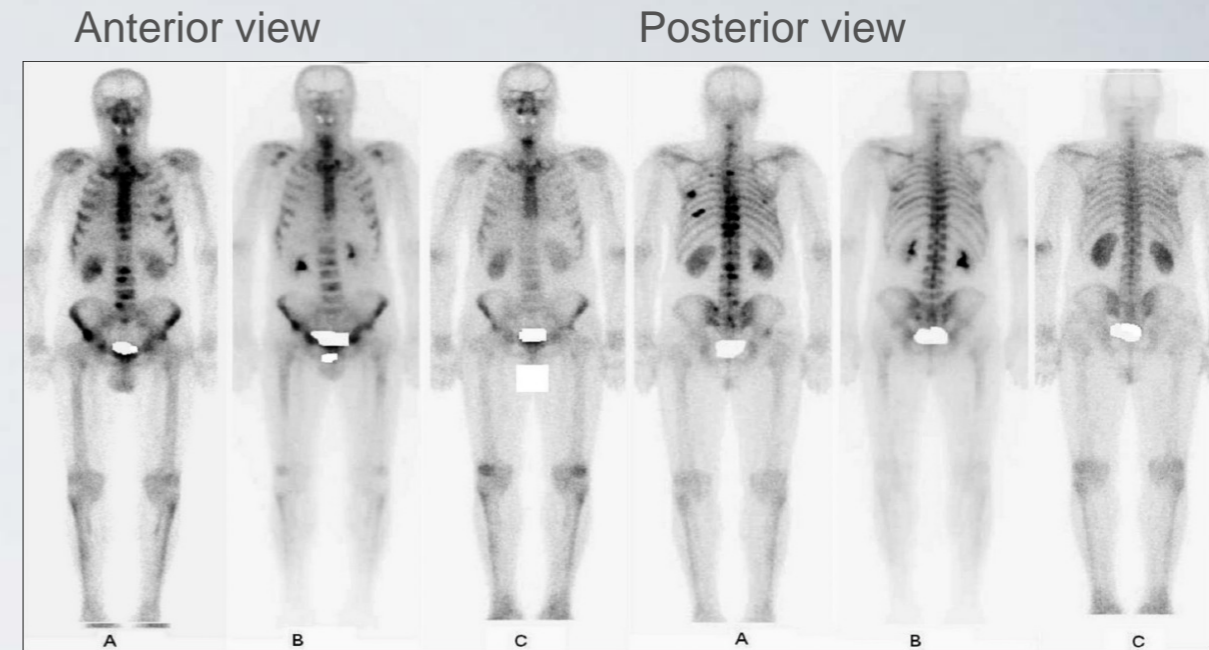
Radio-nuclide	Physical half-life	Mode of decay	Principal E _γ , keV (% intensity)	Max E _{β⁻} , keV (% intensity)	Mean β ⁻ range in soft tissue (mm)	Clinical Indications
³² P	14.26 d	β ⁻		1710	2.6	Polycythemia vera, cystic craniopharyngioma, PVNS
⁸⁹ Sr	50.53 d	β ⁻	910 (0.01)	1496 (100)	2.4	Painful bone metastasis
⁹⁰ Y	64.10 h	β ⁻		2280.1 (100)	3.6	Hepatic metastasis, PVNS, RIT for NHL
^{117m} Sn	13.60 d	IT	158.6 (86)	130*, 150*	0.22, 0.29	Bone tumour treatment
¹³¹ I	8.02 d	β ⁻	364.5 (81.7)	606 (89.3)	0.4	Hyperthyroidism, thyroid cancer, , RIT for NHL and neuroblastoma
¹⁵³ Sm	46.50 h	β ⁻	103.2 (29.8)	808.2 (100)	0.7	Painful bone metastasis, synovitis
¹⁶⁹ Er	9.40 d	β ⁻	84 (0.16)	350	0.3	Synovitis
¹⁷⁷ Lu	6.73 d	β ⁻	208 (11.0)	497.8 (100)	0.28	Synovitis, RIT for various cancer treatments
¹⁸⁶ Re	3.72 d	EC, β ⁻	137 (9.4)	1069.5 (92.5)	1.2	Painful bone metastasis, painful arthritis
¹⁸⁸ Re	17.00 h	β ⁻	155 [(5.1)	2120.4 (100)	2.1	Painful bone metastasis, rheumatoid arthritis, RIT for various cancer treatments
²²³ Ra	11.44 d	α	154 (5.59)	5979.2 ^α	-	Bone metastasis

*conversion electrons; ^αalpha particles

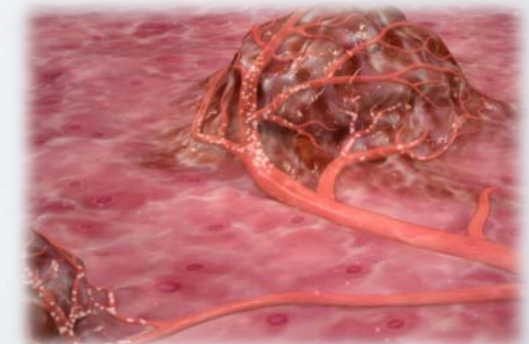
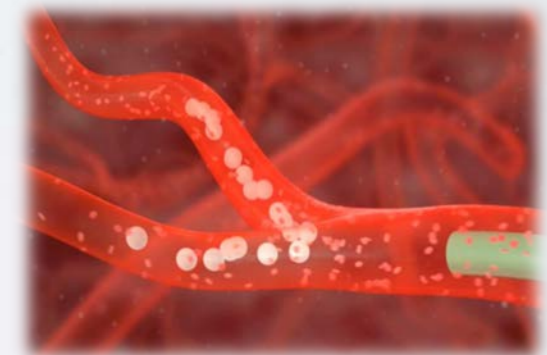
Targeted Radionuclide Therapy

Table 2. Commonly used radiopharmaceuticals for targeted radionuclide therapy

Radiopharmaceutical	Targeting mechanism	Indications
¹³¹ I-Iodide	Thyroid hormone synthesis	Differentiated thyroid cancer Graves' disease Hyperfunctioning nodules
⁹⁰ Y-microspheres	Intravascular trapping	Liver metastasis Hepatocellular carcinoma
⁸⁹ Sr-chloride	Calcium analogue	Bone pain palliation
¹⁵³ Sm-EDTMP	Chemo-adsorption	Bone pain palliation
⁹⁰ Y-Octreotide	Somatostatin receptor binding	Neuroendocrine tumours
¹³¹ I-MIBG	Active transport into neuroendocrine cells and intracellular storage	Neuroblastoma Pheochromocytoma Carcinoid Paraganglioma Medullary thyroid carcinoma

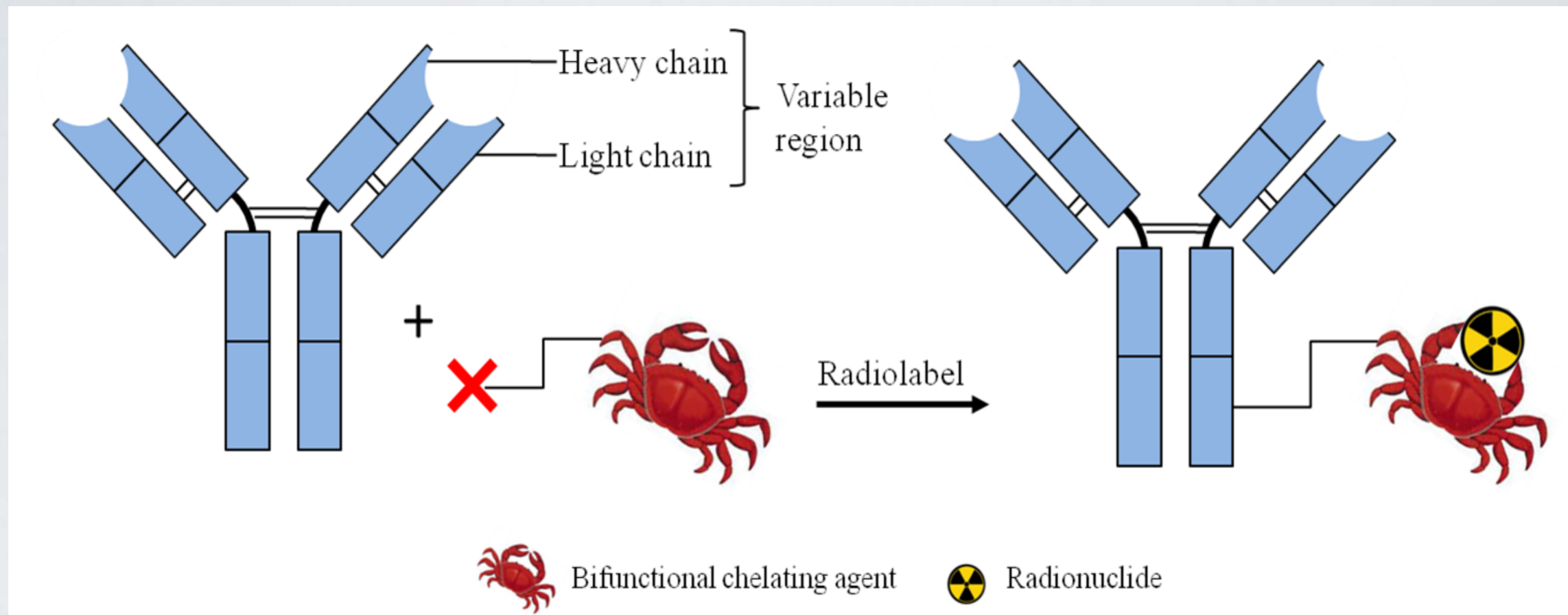


(A) Before; (B) 3 months and (c) 6 months after combined treatment of ¹⁵³Sm Oxabifore and Denosumab



(Courtesy of SIRTEX Medical)

Molecular Targeting Radionuclide Therapy (Radioimmunotherapy or RIT)



RIT is a type of cancer cell targeting therapy which simultaneously utilises monoclonal antibodies (MAbs) labelled with a radionuclide directing against tumour-associated antigens.

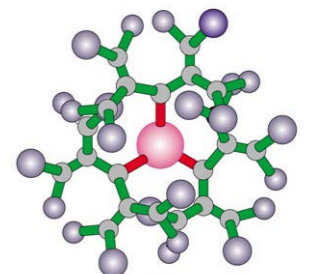
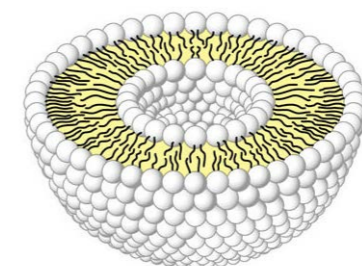
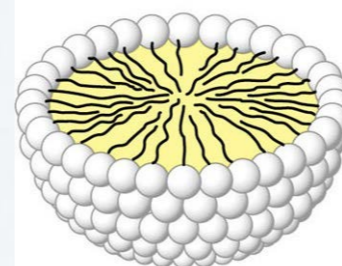
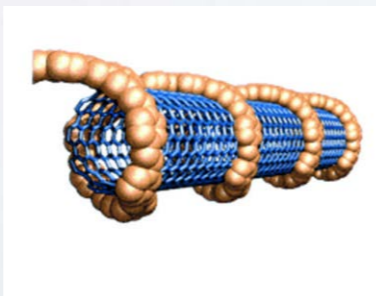
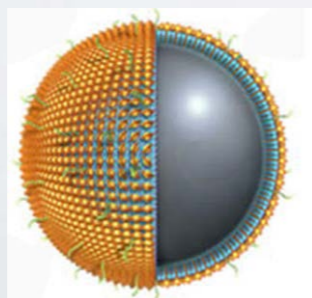
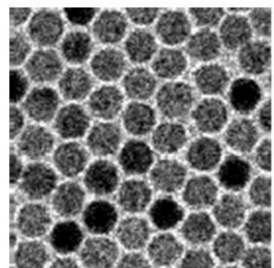
The ability for the antibody to specifically bind to a tumour-associated antigen **increases dose delivered to the tumour cells** while **decreasing dose to normal tissues**.

Table 3. Recently developed monoclonal antibodies for advanced RIA

Name	Antibody form	Radionuclide	Antigen	Disease	Clinical trial status (as of Apr 2014)
Ibritumomab tiuxetan (Zevalin®)	mulgG1	⁹⁰ Y	CD20	NHL	Approved by FDA in 2002; Phase IV
Tositumomab (Bexxar®)	mulgG2a	¹³¹ I	CD20	NHL	Approved by FDA in 2003
Epratuzumab (Lymphocide®)	hulgG1 (LL2)	⁹⁰ Y	CD22	NHL, CLL, immune diseases	Phase III
¹³¹I Lym-1 (Oncolym®)	hulgG1	¹³¹ I	HLA-DR10	NHL, CLL	Phase III
chTNT-1/B (Cotara®)	chlgG1	¹³¹ I	DNA	Glioblastoma multiforme, anaplastic astrocytoma	Phase III
Labetuzumab (CEA-Cide)	hulgG1	⁹⁰ Y or ¹³¹ I	CEA	Breast, lung, pancreatic, stomach and colorectal carcinoma	Pending Phase III
Pemtumomab (Theragyn®)	mulgG1	⁹⁰ Y	PEM	Ovarian, gastric carcinoma	Phase III
¹³¹I-Metuximab (Licartin®)	Hab18 F(ab') ₂	¹³¹ I	Hab18G/CD147	HCC	Phase II
¹³¹I-L19 (Radretumab®)	L19	¹³¹ I	Fibronectin	Hepatological malignancy, refractory Hodgkin's lymphoma, non-small cell lung cancer, melanoma, head and neck carcinoma	Phase II
⁹⁰Y-clivatuzumab tetraxetan (PAM4)	mulgG1	⁹⁰ Y	MUC1	Pancreatic adenocarcinoma	Phase III

Current Issues & Future Prospects

1. Supply issues from nuclear reactors
2. New types of radionuclide generators
3. Molecular biology
4. Theranostics (or “Theragnostics”)
5. Nanotechnology
6. Image-based dosimetry
7. Red marrow dosimetry
8. Radioimmunotherapy vs non-radiolabelled immunotherapy



Conclusion

Therapeutic nuclear medicine is developing **rapidly**. The **non-invasiveness & relatively lower toxicity** make it an attractive and realistic alternative in the management of benign & malignant diseases.

Although there are many challenges ahead, we believe that, with advances in administration methods, a combination of multiple treatment modalities and enhanced therapeutic efficacy, the contribution of therapeutic radionuclides will significantly **increase** in the future.