Nanotechnology and nuclear medicine; research and preclinical applications

Abstract

The birth of nanotechnology in human society was around 2000 years ago and soon found applications in various fields. In this article, we highlight the current status of research and preclinical applications and also future prospects of nanotechnology in medicine and in nuclear medicine. The most important field is cancer. A regular nanotechnology training program for nuclear medicine physicians may be welcome.

Hell J Nucl Med 2011; 14(2): *Published on line: 16 June 2011*

Introduction

Nanotechnology is the manipulation of matter on an atomic and molecular scale to prepare new structures, devices and materials. In general, nanotechnology uses materials sized between 1 and 100 nanometres [1] . The birth of nanotechnology in human society was around 2000 years ago, when sulfide nanocrystals were used as hair dye and gold nanoparticles for coloring glass by ancient Greek and later by Romans [2, 3]. The word "nanos" in Greek means dwarf [2, 3]. Feynman first presented the modern concept of nanotechnology in 1959 [2]. Smalley, who was awarded the Nobel Prize in chemistry for the discovery of a new carbon nanotube, defined nanotechnology "as the art and science of building stuff that does stuff at the nanometer scale"[3]. The interdisciplinary nature of nanotechnology has given it a fundamental influence in various fields, especially medical science. Nanomedicine is defined as the knowledge and skill of manipulating and exploiting the unique chemical, physical, electrical, optical, and biological attributes of natural or synthesized material at the nano-sized scale for various medical purposes, such as opportune prevention, early detection, and targeted treatment of disease [4-9]. Potential nanotargeted radionuclides for diagnosis (Table 1) and treatment (Table 2) are based on the physical half-life, decay mode, the emission properties, and also their tissue penetration range.

Applications of nanotechnology in nuclear medicine can be found in areas of diagnostics, therapeutics, theranostics, and regenerative medicine, as described below (Fig. 1).

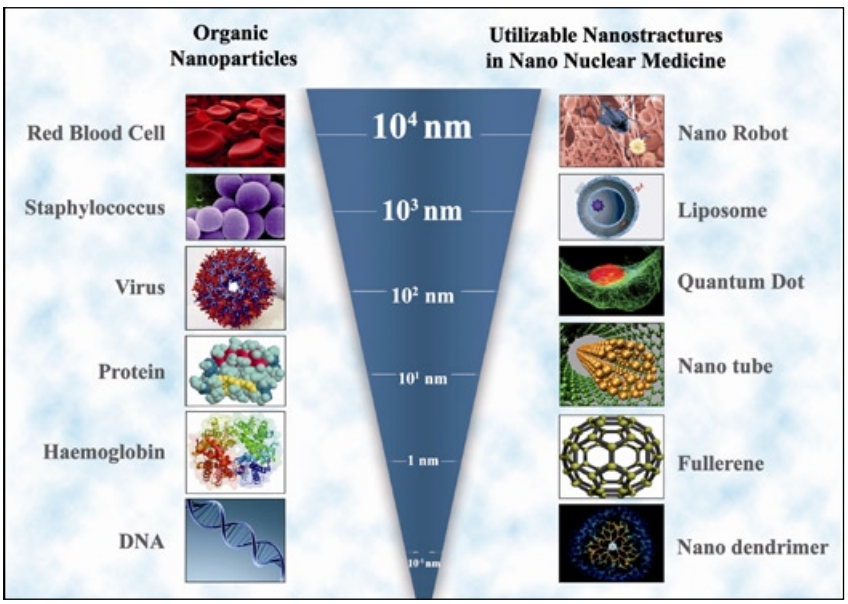

Figure 1. The organic nanoparticle as compared with utilizable nanostructures in nano-nuclear medicine

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Keywords: Nanotechnology
- Nuclear medicine
- Nanomedicine - Theranostic
- Quantum dots (QDs)
- Regenerative medicine

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Received:
27 March 2011
Accepted revised:
1 June 2011

Table 1. *Profiles of potential radionuclides for nanotargeted imaging*

Radionuclide	Emission type	E max(keV)	Half-life	Production	Imaging type
^{99m}Tc	γ	140	6.0h	^{99}Mo/^{99m}Tc-generator	SPET
^{111}In	Auger, γ	171, 245	67.2h	^{111}Cd (p, n) ^{111}In	>>
^{67}Ga	**γ**	93, 184, 300, 393	78.3h	^{68}Zn (n, p) ^{67}Ga	>>
^{131}I	γ (81.2%), β	284, 364, 637	8.0 days	^{130}I(n, γ) ^{131}Te (β) ^{131}I	>>
^{123}I	Auger, γ	159	13.2h	^{121}Sn (α, 2n) ^{123}I	>>
^{125m}Te	γ	-	57.4 days	^{125}Sn(β–) ^{125}Sb(β-)	>>
^{11}C	Positron	960	20.4min	^{14}N (p,α) ^{11}C	PET
^{15}O	>>	1720	2.07min	^{14}N (d,n) ^{15}O	>>
^{13}N	>>	1190	9.96min	^{16}O (p,α) ^{13}N	>>
^{124}I	>>	Eβ+ 2134, 1533	100.2h	^{124}Te(p, n) ^{124}I	>>
^{18}F	>>	Eβ+ 635	1.83h	^{18}O (p, n) ^{18}F	>>
^{76}Br	>>	Eβ+ 3941	16.0h	^{76}Se(p, n) ^{76}Br	>>
^{64}Cu	>>	Eβ+ 656	12.7h	^{64}Ni(p, n)^{64}Cu	>>

EB , E max of β; P, proton; a, alpha; n, neutron

Table 2. *Profiles of potential radionuclides for nanotargeted treatment*

Radionuclide	Emission type	E max (MeV)	Half-life	Production	R max (mean)
^{111}In	Auger,γ	0.42	67h	^{111}Cd (p, n) ^{111}In	2–500nm
^{67}Cu	β	0.19	2.6 d	^{64}Ni(α, p) ^{67}Cu	2.2mm (0.7mm)
^{90}Y	β	2.28	64.1h	^{90}Sr/^{90}Y-generator	12mm (2.8mm)
^{131}I	γ (81.2%), β	0.28, 0.36, 0.64	8 d	^{131}Te (β) ^{131}I	2.4mm (0.8mm)
^{188}Re	β, γ (15.1%)	2.12	17h	^{188}W/^{188}Re-generator	11mm (2.4mm)
^{186}Re	β, γ (9.4%)	1.07	89.2h	^{185}Re (n, γ) ^{186}Re	5mm (1.8mm)
^{225}Ac	α	5.83, 5.79, 5.79, 5.73	10 d	^{225}Ra-generaor	40–80μm
^{177}Lu	β	0.49	161h	^{176}Lu (n, γ) ^{177}Lu	1.6mm (0.67mm)
^{166}Ho	β, γ (6.7%)	1.853	26.9h	^{165}Ho (n, γ) ^{166}Ho	10.2mm
^{89}Sr	β	1.463	52.7 d	^{88}Sr (n,γ) ^{89}Sr	3mm
^{32}P	β	1.71	14.3 d	^{32}S (n,p) ^{32}P or ^{31}P (n, γ) ^{32}P	8.7mm
^{211}At	α	5.87	7.2h	Accelerator	60–80μm
^{213}Bi	α	5.869	45.7min	^{225}Ra-generaor	50–80μm
^{223}Ra	α	-	11.4 d	^{227}Ac-generator	-
^{224}Ra	α	-	3.6 d	generator	-
^{103}Pd	X-ray	0.021	17.0 d	accelerator	-
^{198}Au	β	0.96	2.7 d	cyclotron	-

EB , E max of β; P, proton; a, alpha; n, neutron.

Research and preclinical applications of nanotechnology

Nanomaterials can improve diagnostic imaging techniques even at the level of single cells before overall symptoms appear [7, 10, 11]. Fusion of nanomaterials with molecular imaging devices permits diagnostic and dynamic processes at the molecular level [7]. A single nanoparticle can be tagged with various imaging agents and different targeting ligands can be constructed on similar nanoparticles to introduce selectivity. The ability of nanoparticles to bypass biological barriers enhances targeting efficacy (Fig. 2) [12]. Finally, radio-labeled nanoparticles remain stable under many physiological conditions [13].

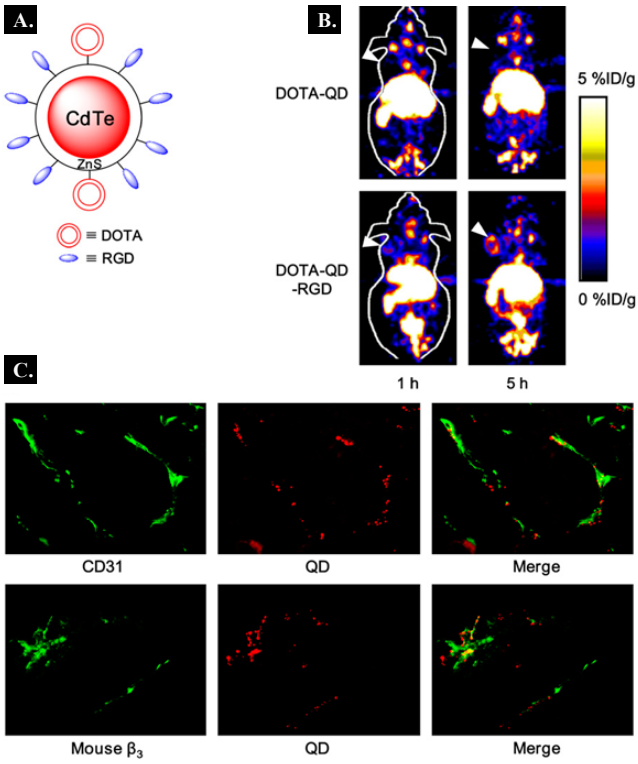

Figure 2. Dual-modality PET/NIRF imaging of integrin αvβ3 in vasculature of tumor. (**A**) A schematic figure of the dual-modality PET/NIRF probe. (**B**) NIRF (after injection of QD-RGD) and coronal microPET (after injection of ^{64}Cu-DOTA-QD-RGD) views of a U87MG tumor bearing mice. (C) Outstanding overlay between CD31 and QD fluorescence, as well as between murine β3 and QD fluorescence, verified that DOTA-QDRGD principally targeted integrin αvβ3 on the tumor vasculature. (Adapted with permission from [12]. ©2007 Society of Nuclear Medicine)

The main advantages of radionuclide-based molecular imaging modalities and of other imaging techniques (e.g. molecular magnetic resonance imaging (mMRI)) are sensitivity, and the possibility of being quantitative, while the main disadvantage is the low resolution typically >1mm [14, 15]. Multimodality imaging using nanoparticles could have a better intrinsic and extrinsic resolution [1, 15] and higher accuracy [12]. Furthermore, multiple imaging agents can be used in multiplexing-modal imaging, simultaneously (Fig. 3) [16]. The enormous surface area of nanoparticles has made them one of the ideal tools to make use of the advantages of multifunctional imaging. Thus nanometric structures can be considered ideal devices for multifunctional imaging programs [17].

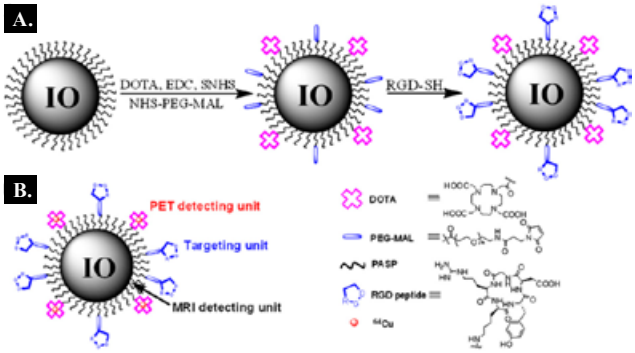

Figure 3. (**A**) Synthesis of PET/MRI dual functional probe DOTA-IO-RGD. DOTA-IO was produced in the same way except that no RGD peptide was used. (**B**) Illustration of PET/MRI probe founded on IO nanoparticle. (Adapted with permission from [16]. ©2008 Society of Nuclear Medicine)

A variety of imaging labels such as superparamagnetic iron oxide (SPIO) nanoparticles**,** quantum dots (QDs), and microbubbles have been used for nuclear imaging of tumor angiogenesis [12][18-21]. Others have suggested that molecular imaging of tumor angiogenesis could be nanomaterial based and be applied also in atherosclerosis and cancer [12].

Multi-labeling of nanoparticles improves contrast-to-noise ratio and eliminates the partial volume effect that is considered a disadvantage of traditional nuclear medicine in the detection of atherosclerosis plaques. Exposed atherosclerosis plaques are an important cause of acute cardiovascular events and sudden death in asymptomatic patients [22]. Furthermore, exchange of high density lipoprotein (HDL) cores with synthetic nanomaterials such as QDs, gold, and iron oxide can be exploited in novel imaging techniques to identify atherosclerotic plaques [23].

Vascular endothelial growth factor (VEGF) as well as the VEGF receptor (VEGFR) and integrin $\alpha_v\beta_3$, due to their important role in angiogenesis and tumor growth, can be applied in cancer diagnostic and therapeutic goals [24-26]. Indium-111 (^{111}In) labeled perfluorocarbon nanoparticles for single photon emission tomography (SPET) imaging of integrin $\alpha_v\beta_3$ in lung carcinoma angiogenesis have revealed that more ^{111}In atoms per nanoparticle reflects an increase in tumor-to-muscle ratio and mean tumor activity [27]. Therefore, this method may be an ideal method to identify newly developed tumors, especially when combined with other techniques [27]. The chemical and biological advantages of nanomaterials make them useful for the transport of contrast agents for nuclear imaging such as ^{99m}Tc, gadolinium, and fluorophores [7].

Quantum dots-based probes, combined with near-infrared fluorescence imaging (NIRF) and positron emission tomography (PET) of integrin $\alpha_v\beta_3$, have quantitatively improved tumor targeting efficacy, so that QD-based NIRF/PET imaging can detect tumors at a lower concentrations than those needed for *in vivo* NIRF imaging [14, 18, 28]. Quantum dots are suitable nanoparticles for cell tracking, reticuloendothelial system mapping, and tumor targeting [29]. Quantum dot-based dual functional NIRF and PET imaging has been applied to evaluate U87MG tumor targeting efficacy [29]. For this purpose, an amine-functionalized QD was linked to VEGF and macrocyclic 1,4,7,10-tetraazacyclododecane-N,N′,N″,N‴,-tetraacetic acid (DOTA) for VEGFR specific binding after ^{64}Cu-labeling for PET imaging. The results showed

Table 3. *Diagnostic applications with radiolabeled nanoparticles*

Nanoparticle	Radionuclide	Kind of imaging	Application
Iron oxide	^{111}In	γ-camera	Breast cancer in mice [69]
Iron oxide	^{64}Cu	PET/MRI	Tumor angiogenesis in animals [16, 70]
Iron oxide	^{124}I	PET/MRI	Lymph node imaging in rats [71, 72]
Iron oxide	^{18}F	Trimodel MRI/PET-CT/optical imaging	In vivo PET-CT imaging in animals [73]
Perfluorocarbon (PFC)	^{111}In	γ-camera	Tumor angiogenesis in rabbits [27, 74]
Carbon nanotube	^{125}I, ^{111}In, ^{86}Y	PET	Distribution in mice [1, 75-79], Targeting of integrin αvβ3-positive tumor in mice [78], multimodality imaging and molecular therapy [27, 80, 81]
Quantum dots	Cd^{125m}Te/ZnS	SPET/CT	Quantitative measurement [82, 83]
Quantum dots	^{64}Cu	PET/NIRF	Tumor angiogenesis PET/NIRF imaging [28, 29, 84-86], human prostate cancer cells growing in live mice [30], nanocrystal HDL into apolipoprotein E in mice (atherosclerosis) [23, 51, 87]
Quantum dots	^{18}F	PET/optical imaging	In vivo multimodal imaging [88], sentinel node mapping [89], in vivo fluorescence imaging (FLI) of the reticuloendothelial system [90]
Liposomes	^{99m}Tc, ^{111}In, ^{67}Ga,	γ-camera	Detection of tumor, infection, inflammation, and lymphoscintigraphy [36, 91-94]
Liposomes	^{111}In	SPET	Clinical biodistribution and also imaging of breast, head and neck, glioma and lung cancers [95, 96], in C-26 tumor-bearing BALB/cByJ mice [36]
Liposomes	^{18}F	PET	In vivo tracking [97-99]
Liposomes	^{111}In, ^{177}Lu	SPET	Tumor targeting for C26 and HT29/luc animal model [98, 100, 101]
Liposomes	^{64}CU	PET	Targeted delivery and imaging with bioconjugated ^{64}Cu-BATPEG-liposome [102]
Immunoliposome	^{111}In	γ-camera	Tumor visualization of murine lewis lung carcinoma and human HT-29 tumors [103-105]
Polymer	^{99m}Tc	γ-camera	Tumor angiogenesis [106]
Dendrimers	^{76}Br	PET	PET imaging of angiogenesis [107]

that the QD-based combination of NIRF and PET imaging significantly enhanced accuracy for the quantitative targeted NIFR imaging [19, 30-32].

Bifunctional PET/MRI imaging of integrin expression using polyaspartic acid (PASP)–coated iron oxide (IO) (PASP-IO) nanoparticles linked to DOTA and cyclic arginine-glycine-aspartic (RGD) peptides resulted in accurate detection of tumor cells in initial stages [16]. The detailed application of radiolabeled nanoparticles in diagnosis is described in Table 3.

Research and preclinical applications of nanotechnology in therapeutics

Currently peptides, viruses, and monoclonal antibodies against tumor molecules are being examined in research and applied as vehicles for specific tumor targeting and effective drug distribution [11, 33, 34]. In addition, several nanoscale liposomes, water-soluble polymers, micelles, and dendrimers are used as nanocarriers in nuclear medicine for diagnostic, therapeutic, and for both diagnostic and therapeutic (theranostic) goals [35][36]. Various genes [37], peptides [38], proteins [39] and antibodies can be tagged with carbon nanotube (CNT) vehicles to target tumor cells [40].

Carbon nanotubes are ideal for drug delivery because they have the ability to transfer effective quantities of radionuclide or drugs [41].

Others used ^{188}Re-(S_3CPh)$_2$(S_2CPH) [^{188}Re-SSS] [(bis(perth iobenzoato)(dithiobenzoato) rhenium-III] trapped in lipid nanocapsules (LNC) as a novel radiopharmaceutical carrier for internal radiotherapy of malignant glioma in Fischer rats. They observed that LNC enhanced the tendency of ^{188}Re to remain in brain tissue. Furthermore, the median survival time of the rats treated with ^{188}Re-SSS LNC was 80% longer than the control group. They proposed that the lipophilic nature of LNC assists in more effective tumor irradiation [42].

Others functionalized epidermal growth factor (EGF) with diethylenepentaacetic acid (DTPA), tagged it with ^{111}In, and used it for the treatment of breast cancer. They observed that the growth rate and survival of hormone-resistant breast cancer cells was significantly reduced [41]. Others functionalized single-walled CNTs with amine groups and DOTA chelating groups.

Chimeric monoclonal antibodies against the CD20 epitope (rituximab) were then appended to the CNT-(DOTA) complex, and tagged with ^{111}In. This bifunctional nanostructure enabled selective targeting of Burkitt's lymphoma cells [43].

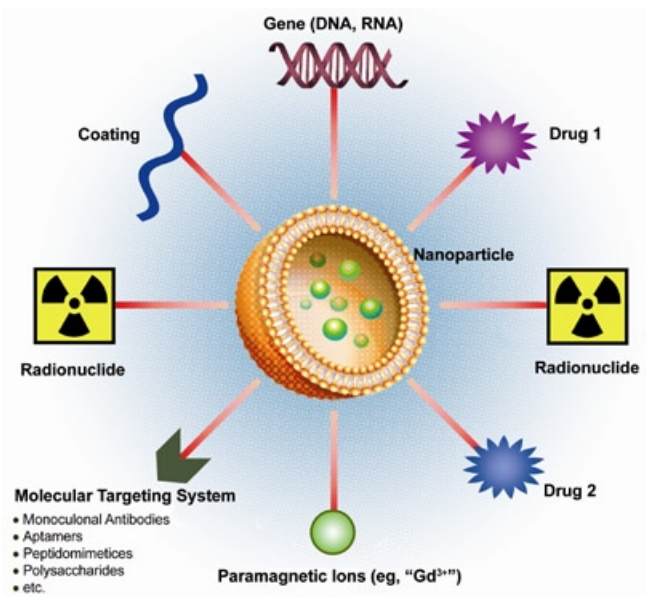

Figure 4. A multifunctional nanoplatform including multimodality imaging, multiple targeting system and multiple therapeutic items

As for theranostics [32] the production of multifunctional nanoparticles has achieved a combination of diagnostic and therapeutic goals simultaneously [44]. Nanomaterial can target a specific site, transport information from the targeted cells, and deliver definite amounts of drug [45-47]. This multifunctional nanoplatforms of nanomedicine seems to play an important role in future [1] (Fig. 4).

Others administered cuprum-64 (^{64}Cu)-labeled folate-conjugated shell cross-linked nanoparticles for PET imaging and radiotherapy of tumor cells [48]. Others placed super-paramagnetic iron oxide nanoparticles (SPION) and ^{18}F-fluoride in haemagglutinating virus of Japan envelops (a vector for gene transferring**)** and compared their distribution with unaltered HVJ-Es when magnets were placed on the heads of injected rodents during PET scanning. It was revealed that magnetic force could change the biodistribution of the viral vehicle. Antibody (mAb)-linked iron oxide nanoparticles (bioprobes) heated by an applied alternating magnetic field (AMF) help to use in tumor specific thermal therapy (Rx) for metastatic cancer (Fig. 5) [49]. This control of biodistribution of therapeutic vehicles has made the site-specific delivery of genes, drugs, and tracers possible [50]. Others have reviewed different nanotechnology applications in molecular imaging and treatment of cardiovascular diseases [51]. Viral vehicles, due to their capability to combine with cell membranes, have been examined for gene delivery [52]. In this field, others studied the M13 virus aimed to help in cancer field [53]. M13 as well as other phages stick to multiple materials. Others have tried to bind M13 to cancer cells at one side and nanodevices known as quantum dots at the other side which could be applied in cancer diagnosis in medical body scans [54]. The detailed application of radiolabeled nanoparticles in treatment is described in Table 4.

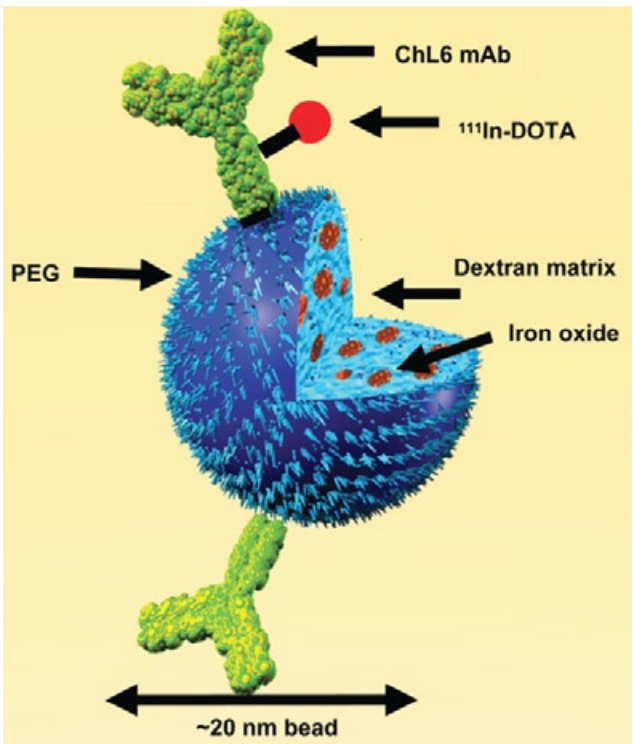

Figure 5. ^{111}In-labeled ChL6 antibody was conjugated to a dextran bead coated with polyethylene glycol and permeated with iron oxide nanoparticles. (Reprinted with permission from [49].©2007 Society of Nuclear Medicine)

Table 4. *Therapeutic applications with radiolabeled nanoparticles*

Nanoparticle	Radionuclide	Treatment	Application
Liposomes	^{131}I,^{67}Cu, ^{198}Au	Radiotherapy	Internal radiotherapy [108-111], nude mice bearing human liver cancer [112], pre-targeted immunotherapy [113], breast cancer [94, 108, 110, 114, 115]
Liposomes	^{90}Y	»	Internal radiotherapy [89, 116-118]
Liposomes	^{186}Re	»	Radionuclide therapy in a head and neck squanous cell carcinoma xenograft positive surgical margin model [119-122]
Liposomes	^{188}Re	»	Ovarian cancer [114], colon cancer in mice [123, 124], internal radiotherapy [8, 124-130]
Liposomes	^{111}In, ^{186}Re	»	Therapeutic efficacy studies of ^{111}In/^{188}Re-liposome on C26 and HT-29 tumor-bearing animal models [123, 131, 132]
Liposomes	^{225}Ac	»	Therapeutic agents for micrometastases cancer [133-136]
Liposomes	^{10}B	»	^{10}B-liposomes nanotargeted therapeutics for boron neutron capture therapy (BNCT) [137, 138]
Liposomes	^{111}In,^{188}Re	Radiochemotherapy	Imaging, biodistribution, pharmacokinetics, therapeutic efficacy, and dosimetry studies of ^{111}In/^{188}Re-VNB/DXR-liposome on C26 and HT-29 tumor/ascites-bearing animal models [122, 124, 129, 130, 132, 139, 140], rat brain tumor model [141]
Immunoliposomes	^{90}Y	Radiotherapy	Therapy with nanotargeted therapeutics of ^{90}Y-DTPA-liposome-IA(integrin antagonist) or ^{90}Y-DTPA-liposome-mAb [118]
Immunoliposomes	^{225}Ac	»	Micrometastases cancer [133-136]
Immunoliposomes and Folate-dendrimers	^{10}B	»	^{10}B-immunoliposomes-anti-EGFR and ^{10}B-PAMAM dendrimers-anti-folate nanotargeted therapeutics for boron neutron capture therapy (BNCT) [142, 143]
Streptavidin	^{111}In	»	^{111}In labeled 3-component streptavidin (^{111}In-MORF/tat/trastuzmab) nanoparticles for auger electron induced antisense-mediated cytoxicity of tumor cells [144]
Dendrimer	^{198}Au	»	melanoma mouse model [145]

Applications in regenerative medicine

Regenerative medicine uses stem cells, induction of endogenous repair mechanisms, or transplantation to restore and repair inefficient tissue with functionality to treat debilitating disorders such as cancer, diabetes, cardiovascular, central or peripheral nerve damage, and osteoarthritic diseases [55, 56].

Quantum dots (QD), iron oxide (IO) nanoparticles, and nano-polymers are favorable materials for regenerative nanomedicine. They can be fused with radioisotopes and used for nuclear-medical procedures. Quantum dots are made from a heavy-metal core cadmium selenic (CdSe), telluric cadmium (CdTe) encircled with a sulfuric zinc (ZnS) shell [56]. The thickness of the shell can be prepared depending on the reaction time.

Semiconductor nanocrystals like QD are used for cell labeling, cell tracking, imaging and monitoring of cellular events [57]. Furthermore QD can mark multiple parts of cells synchronously and can be used in multiplex imaging for biological application [58, 59]. They are also a good option for long-term labeling of stem cell progenitors [58] .

Iron oxide nanoparticles can bind to external cell surfaces and easily separate, or can penetrate into a cell without affecting its viability [60]. A dextran-coated superparamag-

netic iron oxide (SPION) is an appropriate contrast agent for labeling human mesenchymal stem cells (MSC) and human embryonic stem cells (ESC) [61]. Others successfully determined the site of damaged brain cells after brain trauma in a human patient using mesenchymal stem cells (MSC) labeled with superparamagnetic iron oxide (SPION) [62]. Recent studies of SPION-labeled stem cells in cardiovascular system have been promising [63].

Artificial extracellular matrixes, which mimic the structure of natural matrixes, have a critical role in tissue engineering [64]. Nano-fibrous scaffolds function as a mechanical trellis, and can increase the survival of implanted stem cells, which are the key operators in regenerative medicine. They also help to determine the location of transferred stem cells or even can monitor their proliferation, differentiation, and viability [65, 66]. Sodium iodide symporter (NIS) is a membrane protein which can facilitate ^{99m}Tc-pertechnetate imaging [65]. For instance, a research group combined regenerative medicine with nanotechnology and nuclear medicine [65]. They designed MSC expressing the human NIS gene which has been used to estimate the viability of transplanted human stem cells. Scintigraphy has indicated that radionuclide uptake of an MSC-NIS/ poly L-lactic acid (PLLA) complex was higher than MSC-NIS not implanted in a scaffold. Mice treated with an MSC-NIS/PLLA scaffold mixture exhibited higher survival rates than controls treated with non-scaffold MSC-NIS. Scaffold of NSC-fluc/polymer and MSC-NIS/polymer scaffold complexes are valuable candidates for serial *in vivo* imaging and can be used for longitudinal monitoring of implanted stem cells [65] .

The final aim of nanomedicine is that nanoparticle-based agents could be utilized for simultaneous diagnosis and treatment (theranostics), although much remains to be done before nanomedicine can be used in clinical practice [67, 68] (Fig. 6).

In conclusion, nanotechnology in our days is a broad field for medicine and nuclear medicine theranostics, which is expected to yield practical applications in the future.

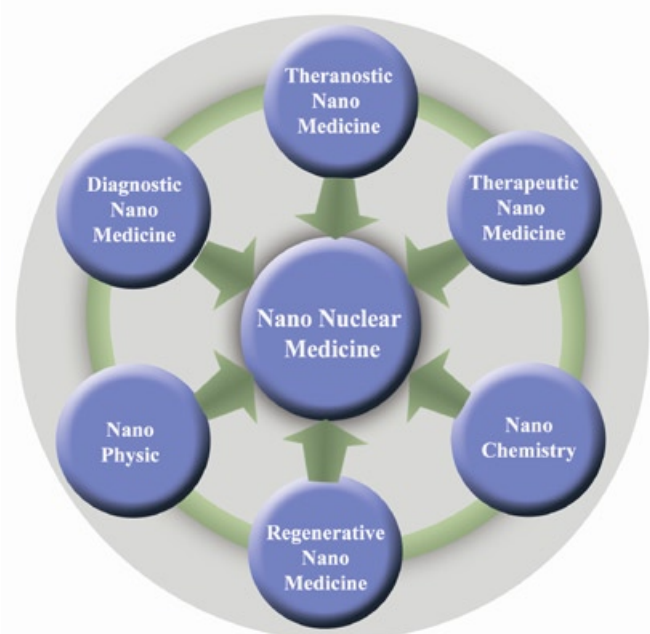

Figure 6. The proposed nano-nuclear medicine and related fields

The author(s) declare that they have no conflicts of interest.

Bibliography

1. Hong H, Zhang Y, Sun J et al. Molecular imaging and therapy of cancer with radiolabeled nanoparticles. *Nano Today* 2009; 4: 399-413.
2. Edwards sa. The visionries. *The nanotech pioneers: Where are they taking us?* Weinheim: Wiley-VCH; 2006:15.
3. Smalley re. Fullerenes, space, and the world's energy challenge. *Caneus 2002: Canada-Europe-US-Japan workshop on micro nano technology for aerospace applications*. Montreal, Ca 2002.
4. Nanomedicine -An ESF- European Medical Research Councils (EMRC) Forward Look Report. Strasbourg cedex,: European Science Foundation; 2004.
5. Monteiro ML, Swanson RA, Coppeto JR et al. A microangiopathic syndrome of encephalopathy, hearing loss, and retinal arteriolar occlusions. *Neurology* 1985; 35: 1113-21.
6. Moghimi SM, Hunter AC, Murray JC. Nanomedicine: current status and future prospects. *FASEB J* 2005; 19: 311-30.
7. Pan D, Lanza GM, Wickline SA et al. Nanomedicine: perspective and promises with ligand-directed molecular imaging. *Eur J Radiol* 2009; 70: 274-85.
8. Ting G, Chang CH, Wang HE et al. Nanotargeted radionuclides for cancer nuclear imaging and internal radiotherapy. *J Biomed Biotechnol* 2010: 9(5): 35-7.
9. Assadi M, Afrasiabi K. An establishment of nano-nuclear medicine fellowship: is it necessary? *Iranian Journal of Nuclear Medicine* 2010; 18(Suppl 1): 67.
10. Assadi M, Nabipour I. The role of nanotechnology in nuclear medicine as a limb of molecular medicine with emphasis on medical roadmap of Iran. *International congress of nuclear medicine and molecular imaging*. Iran; 2009.
11. N*anotechnology*. European technology platform on nanomedicine nanotechnology for health 2005 [cited 2010 June 10].
12. Cai W, Chen X. Multimodality molecular imaging of tumor angiogenesis. *J Nucl Med* 2008; 49 Suppl 2: 113S-28S.
13. Singh R, Pantarotto D, Lacerda L et al. Tissue biodistribution and blood clearance rates of intravenously administered carbon nanotube radiotracers. *Proc Natl Acad Sci U SA* 2006; 103: 3357-62.
14. Massoud TF, Gambhir SS. Molecular imaging in living subjects: seeing fundamental biological processes in a new light. *Genes Dev* 2003; 17: 545-80.
15. Gambhir SS. Molecular imaging of cancer with positron emission tomography. *Nat Rev Cancer* 2002; 2: 683-93.
16. Lee HY, Li Z, Chen K et al. PET/MRI dual-modality tumor imaging using arginine-glycine-aspartic (RGD)-conjugated radiolabeled iron oxide nanoparticles. *J Nucl Med* 2008; 49: 1371-9.
17. Cai W, Chen X. Nanoplatforms for targeted molecular imaging in living subjects. *Small* 2007; 3: 1840-54.
18. Michalet X, Pinaud FF, Bentolila LA et al. Quantum dots for live cells, in vivo imaging, and diagnostics. *Science* 2005; 307: 538-44.
19. Medintz IL, Uyeda HT, Goldman ER et al. Quantum dot bioconjugates for imaging, labelling and sensing. *Nat Mater* 2005; 4: 435-46.
20. Larson DR, Zipfel WR, Williams RM et al. Water-soluble quantum dots for multiphoton fluorescence imaging in vivo. *Science* 2003; 300: 1434-6.
21. Schipper ML, Cheng Z, Lee SW et al. MicroPET-based biodistribution of quantum dots in living mice. *J Nucl Med* 2007; 48: 1511-8.

22. Wagenaar DJ, Chen JA. Nuclear imaging of vulnerable plaque: contrast improvements through multi-labeling of nanoparticles. *Nuclear science symposium conference record, 2005 IEEE*. fajardo; 2005: 5pp.-1685.
23. Cormode DP, Skajaa T, van Schooneveld MM et al. Nanocrystal core high-density lipoproteins: a multimodality contrast agent platform. *Nano Lett* 2008; 8: 3715-23.
24. Cai W, Chen K, Mohamedali KA et al. PET of vascular endothelial growth factor receptor expression. *J Nucl Med* 2006; 47: 2048-56.
25. Ferrara N, Hillan KJ, Novotny W. Bevacizumab (Avastin), a humanized anti-VEGF monoclonal antibody for cancer therapy. *Biochem Biophys Res Commun* 2005; 333: 328-35.
26. Hood JD, Cheresh DA. Role of integrins in cell invasion and migration. *Nat Rev Cancer* 2002; 2: 91-100.
27. Hu G, Lijowski M, Zhang H et al. Imaging of Vx-2 rabbit tumors with alpha(nu)beta3-integrin-targeted ^{111}In nanoparticles. *Int J Cancer* 2007; 120: 1951-7.
28. Cai W, Chen K, Li ZB et al. Dual-function probe for PET and near-infrared fluorescence imaging of tumor vasculature. *J Nucl Med* 2007; 48: 1862-70.
29. Chen K, Li ZB, Wang H et al. Dual-modality optical and positron emission tomography imaging of vascular endothelial growth factor receptor on tumor vasculature using quantum dots. *Eur J Nucl Med Mol Imaging* 2008; 35: 2235-44.
30. Gao X, Cui Y, Levenson RM et al. In vivo cancer targeting and imaging with semiconductor quantum dots. *Nat Biotechnol* 2004; 22: 969-76.
31. Lim YT, Kim S, Nakayama A et al. Selection of quantum dot wavelengths for biomedical assays and imaging. *Mol Imaging* 2003; 2: 50-64.
32. Jackson H, Muhammad O, Daneshvar H et al. Quantum dots are phagocytized by macrophages and colocalize with experimental gliomas. *Neurosurgery* 2007; 60: 524-9; discussion 529-30.
33. Debbage P, Jaschke W. Molecular imaging with nanoparticles: giant roles for dwarf actors. *Histochem Cell Biol* 2008; 130: 845-75.
34. Reilly RM. biomolecules as targeting vehicles for in situ radiotherapy of malignancies. modern biopharmaceuticals: designe, development and optimization, Ed. Knaeblein J. Vol. 2. 2005, Weinheim, Germany: Wiley-VCH.
35. Mitra A, Nan A, Line BR et al. Nanocarriers for nuclear imaging and radiotherapy of cancer. *Curr Pharm Des* 2006; 12: 4729-49.
36. Hamoudeh M, Kamleh MA, Diab R et al. Radionuclides delivery systems for nuclear imaging and radiotherapy of cancer. *Adv Drug Deliv Rev* 2008; 60: 1329-46.
37. Pantarotto D, Singh R, McCarthy D et al. Functionalized carbon nanotubes for plasmid DNA gene delivery. *Angew Chem Int Ed Engl* 2004; 43: 5242-6.
38. Pantarotto D, Briand JP, Prato M et al. Translocation of bioactive peptides across cell membranes by carbon nanotubes. *Chem Commun (Camb)* 2004; 16-7.
39. Kam NW, O'Connell M, Wisdom JA et al. Carbon nanotubes as multifunctional biological transporters and near-infrared agents for selective cancer cell destruction. *Proc Natl Acad Sci U SA* 2005; 102(11): 600-5.
40. Reilly RM. Carbon nanotubes: potential benefits and risks of nanotechnology in nuclear medicine. *J Nucl Med* 2007; 48: 1039-42.
41. Reilly R. The immunoreactivity of radiolabeled antibodies--its impact on tumor targeting and strategies for preservation. *Cancer Biother Radiopharm* 2004; 19: 669-72.
42. Allard E, Hindre F, Passirani C et al. ^{188}Re-loaded lipid nanocapsules as a promising radiopharmaceutical carrier for internal radiotherapy of malignant gliomas. *Eur J Nucl Med Mol Imaging* 2008; 35: 1838-46.
43. McDevitt MR, Chattopadhyay D, Kappel BJ et al. Tumor targeting with antibody-functionalized, radiolabeled carbon nanotubes. *J Nucl Med* 2007; 48: 1180-9.
44. Lucignani G. Nanoparticles for concurrent multimodality imaging and therapy: the dawn of new theragnostic synergies. *Eur J Nucl Med Mol Imaging* 2009; 36: 869-74.
45. Pastorin G, Wu W, Wieckowski S et al. Double functionalization of carbon nanotubes for multimodal drug delivery. *Chem Commun (Camb)* 2006; 1182-4.
46. Kim G, O'Regan R, Nie S. Biomedical nanotechnology for molecular imaging, profiling, and drug targeting. *Conf Proc IEEE Eng Med Biol Soc* 2005; 1: 714-6.
47. Longmire M, Choyke PL, Kobayashi H. Clearance properties of nano-sized particles and molecules as imaging agents: considerations and caveats. *Nanomedicine (Lond)* 2008; 3: 703-17.
48. Rossin R, Pan D, Qi K et al. ^{64}Cu-labeled folate-conjugated shell cross-linked nanoparticles for tumor imaging and radiotherapy: synthesis, radiolabeling, and biologic evaluation. *J Nucl Med* 2005; 46: 1210-8.
49. DeNardo SJ, DeNardo GL, Natarajan A et al. Thermal dosimetry predictive of efficacy of ^{111}In-ChL6 nanoparticle AMF--induced thermoablative therapy for human breast cancer in mice. *J Nucl Med* 2007; 48: 437-44.
50. Flexman JA, Cross DJ, Lewellen BL et al. Magnetically targeted viral envelopes: a PET investigation of initial biodistribution. *IEEE Trans Nanobioscience* 2008; 7: 223-32.
51. Wickline SA, Neubauer AM, Winter PM et al. Molecular imaging and therapy of atherosclerosis with targeted nanoparticles. *J Magn Reson Imaging* 2007; 25: 667-80.
52. Galanis E, Vile R, Russell SJ. Delivery systems intended for in vivo gene therapy of cancer: targeting and replication competent viral vectors. *Crit Rev Oncol Hematol* 2001; 38: 177-92.
53. Ross PE. Viral nano electronics. *Sci Am* 2006; 295: 52-5.
54. Lee SW, Mao C, Flynn CE et al. Ordering of quantum dots using genetically engineered viruses. *Science* 2002; 296: 892-5.
55. Muneoka K, Allan CH, Yang X et al. Mammalian regeneration and regenerative medicine. *Birth Defects Res C Embryo Today* 2008; 84: 265-80.
56. Solanki A, Kim JD, Lee KB. Nanotechnology for regenerative medicine: nanomaterials for stem cell imaging. *Nanomedicine (Lond)* 2008; 3: 567-78.
57. Rosen AB, Kelly DJ, Schuldt AJ et al. Finding fluorescent needles in the cardiac haystack: tracking human mesenchymal stem cells labeled with quantum dots for quantitative in vivo three-dimensional fluorescence analysis. *Stem Cells* 2007; 25: 2128-38.
58. Jaiswal JK, Mattoussi H, Mauro JM et al. Long-term multiple color imaging of live cells using quantum dot bioconjugates. *Nat Biotechnol* 2003; 21: 47-51.
59. Wu X, Liu H, Liu J et al. Immunofluorescent labeling of cancer marker Her2 and other cellular targets with semiconductor quantum dots. *Nat Biotechnol* 2003; 21: 41-6.
60. Bulte JW, Kraitchman DL. Monitoring cell therapy using iron oxide MR contrast agents. *Curr Pharm Biotechnol* 2004; 5: 567-84.
61. Corot C, Robert P, Idee JM et al. Recent advances in iron oxide nanocrystal technology for medical imaging. *Adv Drug Deliv Rev* 2006; 58: 1471-504.
62. Zhu J, Zhou L, XingWu F. Tracking neural stem cells in patients with brain trauma. *N Engl J Med* 2006; 355: 2376-8.
63. Kraitchman DL, Heldman AW, Atalar E et al. In vivo magnetic resonance imaging of mesenchymal stem cells in myocardial infarction. *Circulation* 2003; 107: 2290-3.

64. Li X, Liu X, Dong W et al. In vitro evaluation of porous poly(L-lactic acid) scaffold reinforced by chitin fibers. *J Biomed Mater Res B Appl Biomater* 2009; 90: 503-9.
65. Hwang do W, Jang SJ, Kim YH et al. Real-time in vivo monitoring of viable stem cells implanted on biocompatible scaffolds. *Eur J Nucl Med Mol Imaging* 2008; 35: 1887-98.
66. Park KI, Teng YD, Snyder EY. The injured brain interacts reciprocally with neural stem cells supported by scaffolds to reconstitute lost tissue. *Nat Biotechnol* 2002; 20: 1111-7.
67. Del Vecchio S, Zannetti A, Fonti R et al. Nuclear imaging in cancer theranostics. *Q J Nucl Med Mol Imaging* 2007; 51: 152-63.
68. Sumer B, Gao J. Theranostic nanomedicine for cancer. *Nanomedicine (Lond)* 2008; 3: 137-40.
69. DeNardo SJ, DeNardo GL, Miers LA et al. Development of tumor targeting bioprobes (^{111}In-chimeric L6 monoclonal antibody nanoparticles) for alternating magnetic field cancer therapy. *Clin Cancer Res* 2005; 11: 7087s-7092s.
70. Jarrett BR, Gustafsson B, Kukis DL et al. Synthesis of ^{64}Cu-labeled magnetic nanoparticles for multimodal imaging. *Bioconjug Chem* 2008; 19: 1496-504.
71. Choi JS, Park JC, Nah H et al. A hybrid nanoparticle probe for dual-modality positron emission tomography and magnetic resonance imaging. *Angew Chem Int Ed Engl* 2008; 47: 6259-62.
72. Bogenrieder T, Herlyn M. Axis of evil: molecular mechanisms of cancer metastasis. *Oncogene* 2003; 22: 6524-36.
73. Devaraj NK, Keliher EJ, Thurber GM et al. ^{18}F labeled nanoparticles for in vivo PET-CT imaging. *Bioconjug Chem* 2009; 20: 397-401.
74. Tran TD, Caruthers SD, Hughes M et al. Clinical applications of perfluorocarbon nanoparticles for molecular imaging and targeted therapeutics. *Int J Nanomedicine* 2007; 2: 515-26.
75. Wang H, Wang J, Deng X et al. Biodistribution of carbon single-wall carbon nanotubes in mice. *J Nanosci Nanotechnol* 2004; 4: 1019-24.
76. Balasubramanian K, Burghard M. Chemically functionalized carbon nanotubes. *Small* 2005; 1: 180-92.
77. Lacerda L, Bianco A, Prato M et al. Carbon nanotubes as nanomedicines: from toxicology to pharmacology. *Adv Drug Deliv Rev* 2006; 58: 1460-70.
78. Liu Z, Cai W, He L et al. In vivo biodistribution and highly efficient tumour targeting of carbon nanotubes in mice. *Nat Nanotechnol* 2007; 2: 47-52.
79. McDevitt MR, Chattopadhyay D, Jaggi JS et al. PET imaging of soluble yttrium-86-labeled carbon nanotubes in mice. *PLoS One* 2007; 2: e907.
80. Liu Z, Chen K, Davis C et al. Drug delivery with carbon nanotubes for in vivo cancer treatment. *Cancer Res* 2008; 68: 6652-60.
81. Joshi BP, Wang TD. Exogenous Molecular Probes for Targeted Imaging in Cancer: Focus on Multi-modal Imaging. *Cancers* 2010; 2: 1251-87.
82. Pelley JL, Daar AS, Saner MA. State of academic knowledge on toxicity and biological fate of quantum dots. *Toxicol Sci* 2009; 112: 276-96.
83. Kennel SJ, Woodward JD, Rondinone AJ et al. The fate of MAb-targeted Cd(125m)Te/ZnS nanoparticles in vivo. *Nucl Med Biol* 2008; 35: 501-14.
84. Cai W, Shin DW, Chen K et al. Peptide-labeled near-infrared quantum dots for imaging tumor vasculature in living subjects. *Nano Lett* 2006; 6: 669-76.
85. Bentolila LA, Ebenstein Y, Weiss S. Quantum dots for in vivo small-animal imaging. *J Nucl Med* 2009; 50: 493-6.
86. Wu Y, Zhang X, Xiong Z et al. microPET imaging of glioma integrin {alpha}v{beta}3 expression using ^{64}Cu-labeled tetrameric RGD peptide. *J Nucl Med* 2005; 46: 1707-18.
87. Mulder WJ, Cormode DP, Hak S et al. Multimodality nanotracers for cardiovascular applications. *Nat Clin Pract Cardiovasc Med* 2008; 5 Suppl 2: S103-11.
88. Duconge F, Pons T, Pestourie C et al. Fluorine-18-labeled phospholipid quantum dot micelles for in vivo multimodal imaging from whole body to cellular scales. *Bioconjug Chem* 2008; 19: 1921-6.
89. Kim S, Lim YT, Soltesz EG et al. Near-infrared fluorescent type II quantum dots for sentinel lymph node mapping. *Nat Biotechnol* 2004; 22: 93-7.
90. Inoue Y, Izawa K, Yoshikawa K et al. In vivo fluorescence imaging of the reticuloendothelial system using quantum dots in combination with bioluminescent tumour monitoring. *Eur J Nucl Med Mol Imaging* 2007; 34: 2048-56.
91. Boerman OC, Laverman P, Oyen WJ et al. Radiolabeled liposomes for scintigraphic imaging. *Prog Lipid Res* 2000; 39: 461-75.
92. Ogihara-Umeda I, Sasaki T, Kojima S et al. Optimal radiolabeled liposomes for tumor imaging. *J Nucl Med* 1996; 37: 326-32.
93. Phillips WT. Delivery of gamma-imaging agents by liposomes. *Adv Drug Deliv Rev* 1999; 37: 13-32.
94. Dagar S, Krishnadas A, Rubinstein I et al. VIP grafted sterically stabilized liposomes for targeted imaging of breast cancer: in vivo studies. *J Control Release* 2003; 91: 123-33.
95. Harrington KJ, Mohammadtaghi S, Uster PS et al. Effective targeting of solid tumors in patients with locally advanced cancers by radiolabeled pegylated liposomes. *Clin Cancer Res* 2001; 7: 243-54.
96. Harrington KJ, Lewanski CR, Stewart JS. Liposomes as vehicles for targeted therapy of cancer. Part 1: preclinical development. *Clin Oncol (R Coll Radiol)* 2000; 12: 2-15.
97. Urakami T, Akai S, Katayama Y et al. Novel amphiphilic probes for ^{18}F-radiolabeling preformed liposomes and determination of liposomal trafficking by positron emission tomography. *J Med Chem* 2007; 50: 6454-7.
98. Oku N. Delivery of contrast agents for positron emission tomography imaging by liposomes. *Adv Drug Deliv Rev* 1999; 37: 53-61.
99. Marik J, Tartis MS, Zhang H et al. Long-circulating liposomes radiolabeled with [18F]fluorodipalmitin (^{18}F-FDP). *Nucl Med Biol* 2007; 34: 165-71.
100. Wang H-E, Yu H-M, Lu Y-C et al. Internal radiotherapy and dosimetric study for ^{111}In/^{177}Lu-pegylated liposomes conjugates in tumor-bearing mice. *Nuclear Instruments and Methods in Physics Research A* 2006; 569: 533-7.
101. Lee W-C, Hwang J-J, Tseng Y-L et al. Therapeutic e cacy evaluation of ^{111}In-VNB-liposome on human colorectal adenocarcinoma HT-29/luc mouse xenografts. *Nuclear Instruments and Methods in Physics Research A* 2006; 596: 497-504.
102. Seo JW, Zhang H, Kukis DL et al. A novel method to label preformed liposomes with ^{64}Cu for positron emission tomography (PET) imaging. *Bioconjug Chem* 2008; 19: 2577-84.
103. Elbayoumi TA, Pabba S, Roby A et al. Antinucleosome antibody-modified liposomes and lipid-core micelles for tumor-targeted delivery of therapeutic and diagnostic agents. *J Liposome Res* 2007; 17: 1-14.
104. Elbayoumi TA, Torchilin VP. Enhanced accumulation of long-circulating liposomes modified with the nucleosome-specific monoclonal antibody 2C5 in various tumours in mice: gamma-imaging studies. *Eur J Nucl Med Mol Imaging* 2006; 33: 1196-205.
105. Erdogan S, Roby A, Torchilin VP. Enhanced tumor visualization by gamma-scintigraphy with ^{111}In-labeled polychelating-polymer-containing immunoliposomes. *Mol Pharm* 2006; 3: 525-30.

106. Line BR, Mitra A, Nan A et al. Targeting tumor angiogenesis: comparison of peptide and polymer-peptide conjugates. *J Nucl Med* 2005; 46: 1552-60.
107. Almutairi A, Rossin R, Shokeen M et al. Biodegradable dendritic positron-emitting nanoprobes for the noninvasive imaging of angiogenesis. *Proc Natl Acad Sci U SA* 2009; 106: 685-90.
108. Emfietzoglou D, Kostarelos K, Sgouros G. An analytic dosimetry study for the use of radionuclide-liposome conjugates in internal radiotherapy. *J Nucl Med* 2001; 42: 499-504.
109. Seymour L, Eisenhauer E. A review of dose-limiting events in phase I trials: antimetabolites show unpredictable relationships between dose and toxicity. *Cancer Chemother Pharmacol* 2001; 47: 2-10.
110. Kostarelos K, Emfietzoglou D. Tissue dosimetry of liposome-radionuclide complexes for internal radiotherapy: toward liposome-targeted therapeutic radiopharmaceuticals. *Anticancer Res* 2000; 20: 3339-45.
111. Hallahan D, Geng L, Qu S et al. Integrin-mediated targeting of drug delivery to irradiated tumor blood vessels. *Cancer Cell* 2003; 3: 63-74.
112. Chen J, Wu H, Han D et al. Using anti-VEGF McAb and magnetic nanoparticles as double-targeting vector for the radioimmunotherapy of liver cancer. *Cancer Lett* 2006; 231: 169-75.
113. Mougin-Degraef M, Bourdeau C, Jestin E et al. Doubly radiolabeled liposomes for pretargeted radioimmunotherapy. *Int J Pharm* 2007; 344: 110-7.
114. Syme AM, McQuarrie SA, Middleton JW et al. Dosimetric model for intraperitoneal targeted liposomal radioimmunotherapy of ovarian cancer micrometastases. *Phys Med Biol* 2003; 48: 1305-20.
115. Emfietzoglou D, Kostarelos K, Papakostas A et al. Liposome-mediated radiotherapeutics within avascular tumor spheroids: comparative dosimetry study for various radionuclides, liposome systems, and a targeting antibody. *J Nucl Med* 2005; 46: 89-97.
116. Burke JM, Jurcic JG, Scheinberg DA. Radioimmunotherapy for acute leukemia. *Cancer Control* 2002; 9: 106-13.
117. Stein R, Chen S, Haim S et al. Advantage of yttrium-90-labeled over iodine-131-labeled monoclonal antibodies in the treatment of a human lung carcinoma xenograft. *Cancer* 1997; 80: 2636-41.
118. Li L, Wartchow CA, Danthi SN et al. A novel antiangiogenesis therapy using an integrin antagonist or anti-Flk-1 antibody coated ^{90}Y-labeled nanoparticles. *Int J Radiat Oncol Biol Phys* 2004; 58: 1215-27.
119. Wang SX, Bao A, Herrera SJ et al. Intraoperative ^{186}Re-liposome radionuclide therapy in a head and neck squamous cell carcinoma xenograft positive surgical margin model. *Clin Cancer Res* 2008; 14: 3975-83.
120. Phillips WT, Klipper R, Goins B. Novel method of greatly enhanced delivery of liposomes to lymph nodes. *J Pharmacol Exp Ther* 2000; 295: 309-13.
121. Zavaleta CL, Goins BA, Bao A et al. Imaging of ^{186}Re-liposome therapy in ovarian cancer xenograft model of peritoneal carcinomatosis. *J Drug Target* 2008; 16: 626-37.
122. Chang CH, Stabin MG, Chang YJ et al. Comparative dosimetric evaluation of nanotargeted ^{188}Re-(DXR)-liposome for internal radiotherapy. *Cancer Biother Radiopharm* 2008; 23: 749-58.
123. Chang YJ, Chang CH, Chang TJ et al. Biodistribution, pharmacokinetics and microSPECT/CT imaging of ^{188}Re-bMEDA-liposome in a C26 murine colon carcinoma solid tumor animal model. *Anticancer Res* 2007; 27: 2217-25.
124. Chen LC, Chang CH, Yu CY et al. Pharmacokinetics, micro-SPECT/CT imaging and therapeutic efficacy of ^{188}Re-DXR-liposome in C26 colon carcinoma ascites mice model. *Nucl Med Biol* 2008; 35: 883-93.
125. Hamoudeh M, Fessi H, Mehier H et al. Dirhenium decacarbonyl-loaded PLLA nanoparticles: influence of neutron irradiation and preliminary in vivo administration by the TMT technique. *Int J Pharm* 2008; 348: 125-36.
126. Chunfu Z, Jinquan C, Duanzhi Y et al. Preparation and radiolabeling of human serum albumin (HSA)-coated magnetite nanoparticles for magnetically targeted therapy. *Appl Radiat Isot* 2004; 61: 1255-9.
127. Hafeli UO. Magnetically modulated therapeutic systems. *Int J Pharm* 2004; 277: 19-24.
128. Liang S, Wang Y, Yu J et al. Surface modified superparamagnetic iron oxide nanoparticles: as a new carrier for bio-magnetically targeted therapy. *J Mater Sci Mater Med* 2007; 18: 2297-302.
129. Chow TH, Lin YY, Hwang JJ et al. Diagnostic and therapeutic evaluation of ^{111}In-vinorelbine-liposomes in a human colorectal carcinoma HT-29/luc-bearing animal model. *Nucl Med Biol* 2008; 35: 623-34.
130. Lin YY, Li JJ, Chang CH et al. Evaluation of pharmacokinetics of ^{111}In-labeled VNB-PEGylated liposomes after intraperitoneal and intravenous administration in a tumor/ascites mouse model. *Cancer Biother Radiopharm* 2009; 24: 453-60.
131. Chen LC, Chang CH, Yu CY et al. Biodistribution, pharmacokinetics and imaging of ^{188}Re-BMEDA-labeled pegylated liposomes after intraperitoneal injection in a C26 colon carcinoma ascites mouse model. *Nucl Med Biol* 2007; 34: 415-23.
132. Chow TH, Lin YY, Hwang JJ et al. Improvement of biodistribution and therapeutic index via increase of polyethylene glycol on drug-carrying liposomes in an HT-29/luc xenografted mouse model. *Anticancer Res* 2009; 29: 2111-20.
133. Chang MY, Seideman J, Sofou S. Enhanced loading efficiency and retention of ^{225}Ac in rigid liposomes for potential targeted therapy of micrometastases. *Bioconjug Chem* 2008; 19: 1274-82.
134. Sofou S, Kappel BJ, Jaggi JS et al. Enhanced retention of the alpha-particle-emitting daughters of Actinium-225 by liposome carriers. *Bioconjug Chem* 2007; 18: 2061-7.
135. Sofou S, Thomas JL, Lin HY et al. Engineered liposomes for potential alpha-particle therapy of metastatic cancer. *J Nucl Med* 2004; 45: 253-60.
136. Henriksen G, Schoultz BW, Michaelsen TE et al. Sterically stabilized liposomes as a carrier for alpha-emitting radium and actinium radionuclides. *Nucl Med Biol* 2004; 31: 441-9.
137. Nakamura H, Ueno M, Ban HS et al. Development of boron nanocapsules for neutron capture therapy. *Appl Radiat Isot* 2009; 67: S84-7.
138. Yanagie H, Maruyama K, Takizawa T et al. Application of boron-entrapped stealth liposomes to inhibition of growth of tumour cells in the in vivo boron neutron-capture therapy model. *Biomed Pharmacother* 2006; 60: 43-50.
139. Lee W-C, Hwang J-J, Tseng Y-L et al. Therapeutic efficacy evaluation of ^{111}In-VNB-liposome on human colorectal adenocarcinoma HT-29/luc mouse xenografts. *Nuclear Instruments and Methods in Physics Research A* 2006; 569: 497-504.
140. Chang YJ, Chang CH, Yu CY et al. Therapeutic efficacy and microSPECT/CT imaging of ^{188}Re-DXR-liposome in a C26 murine colon carcinoma solid tumor model. *Nucl Med Biol* 37: 95-104.
141. Barth RF. Rat brain tumor models in experimental neuro-oncology: the 9L, C6, T9, F98, RG2 (D74), RT-2 and CNS-1 gliomas. *J Neurooncol* 1998; 36: 91-102.

142. Pan X, Wu G, Yang W et al. Synthesis of cetuximab-immunoliposomes via a cholesterol-based membrane anchor for targeting of EGFR. *Bioconjug Chem* 2007; 18: 101-8.
143. Shukla S, Wu G, Chatterjee M et al. Synthesis and biological evaluation of folate receptor-targeted boronated PAMAM dendrimers as potential agents for neutron capture therapy. *Bioconjug Chem* 2003; 14: 158-67.
144. Liu X, Wang Y, Nakamura K et al. Auger radiation-induced, antisense-mediated cytotoxicity of tumor cells using a 3-component streptavidin-delivery nanoparticle with ^{111}In. *J Nucl Med* 2009; 50: 582-90.
145. Khan MK, Minc LD, Nigavekar SS et al. Fabrication of {^{198}Au0} radioactive composite nanodevices and their use for nanobrachytherapy. *Nanomedicine* 2008; 4: 57-69.