Professional Session: Medical Physics Cross-Specialization in the Era of Radiotheranostics

What is Radiotheranostics?

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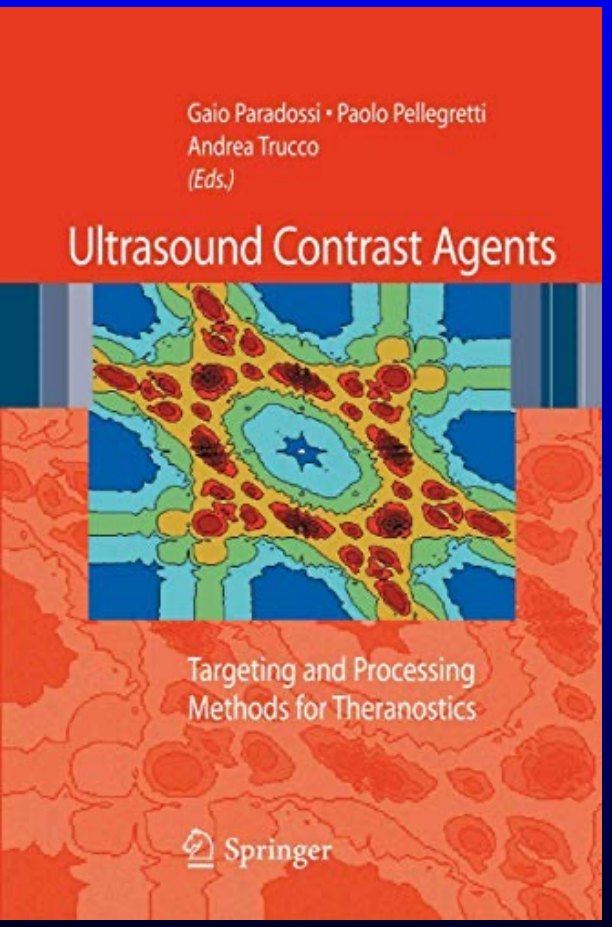
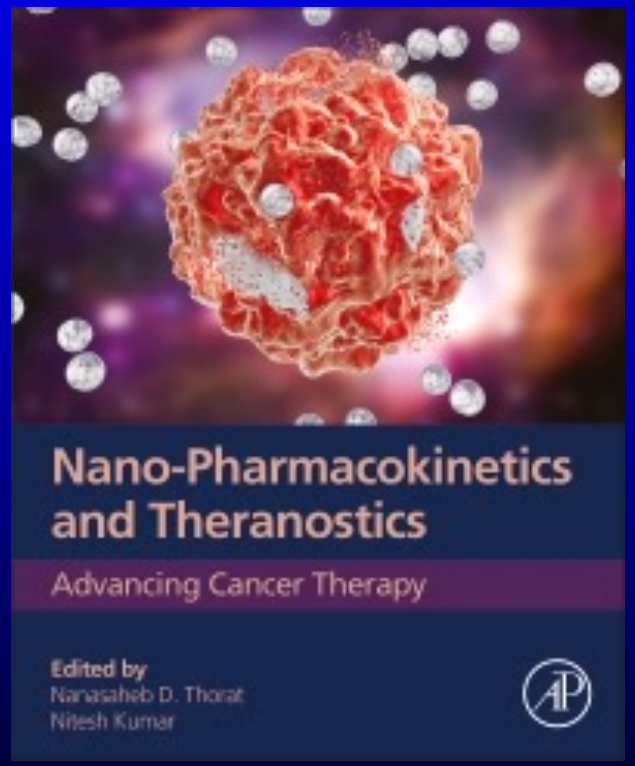
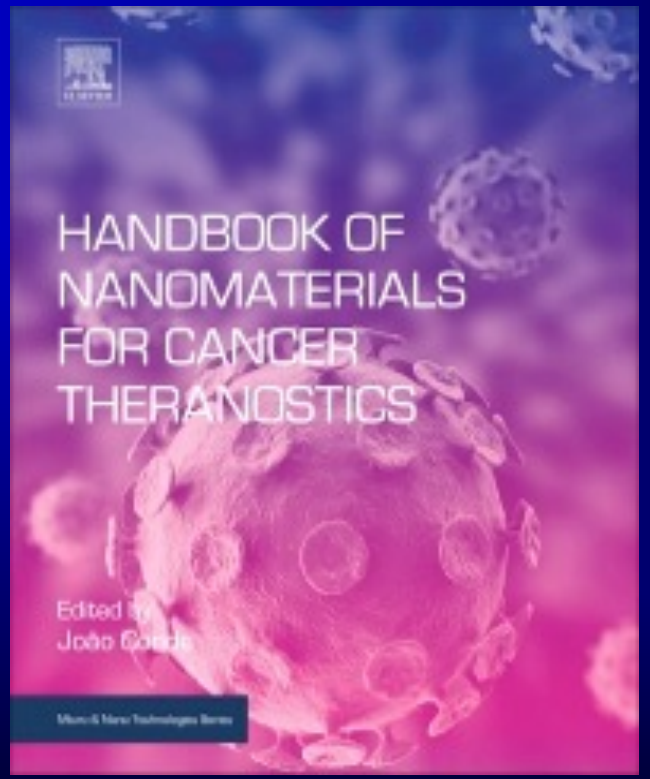
Theranostic Definition

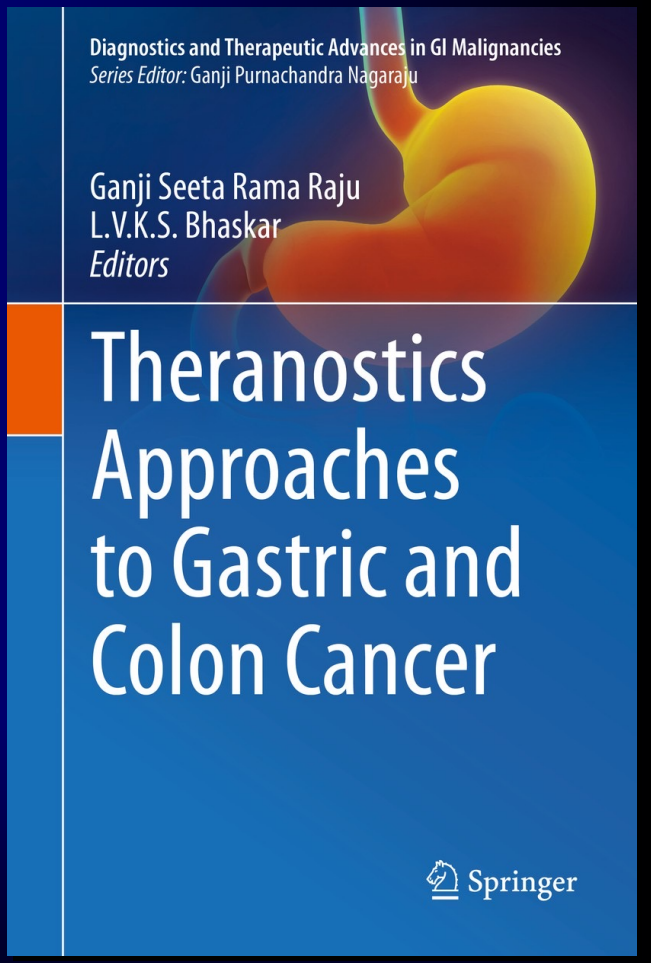
- According to Prof. Dale Bailey, University of Sydney, Australia: The term “theranostic” [thera(py) + (diag)nostic”] is attributed to the American John Funkhouser in a press release from the company Cardiovascular Diagnostics in August 1998
- Theranostics is the pairing of diagnostic biomarkers with therapeutic agents that share a specific target in diseased cells or tissues [Gomes Marin, J et al. 2020, *RadioGraphics*, 40(6)]
- Theranostics do not have to involve radionuclides

Examples of publications on theranostics that do not involve radionuclides





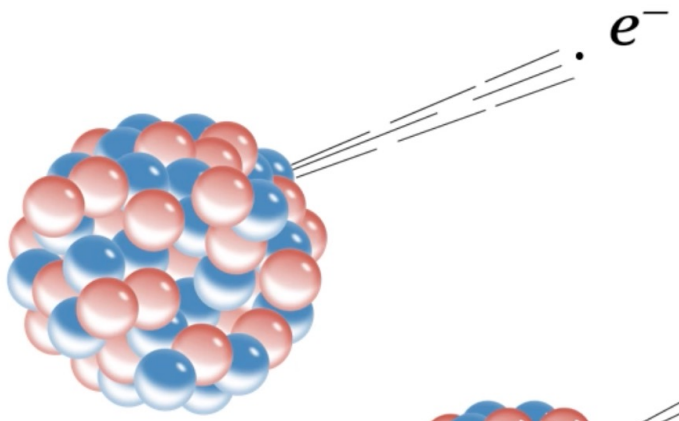




Particles for Theranostics

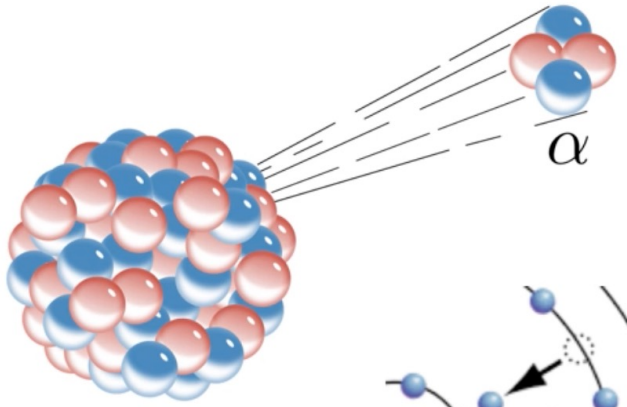
Beta-minus (β^-)

- Examples: ^{32}P, ^{67}Cu, ^{90}Y, ^{131}I, ^{177}Lu, ^{188}Re



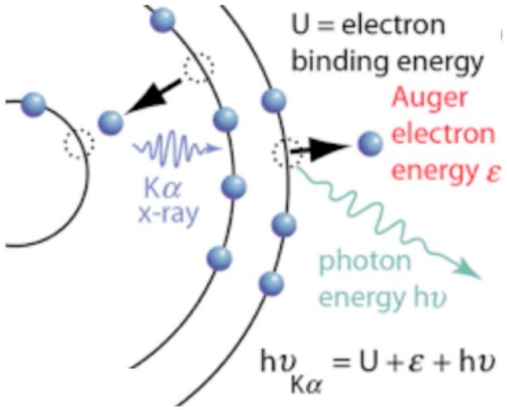
Alpha (α^{2+})

- Examples: ^{149}Tb, ^{210}Pb, ^{213}Bi, ^{223}Ra, ^{225}Ac, ^{227}Th ^{211}At



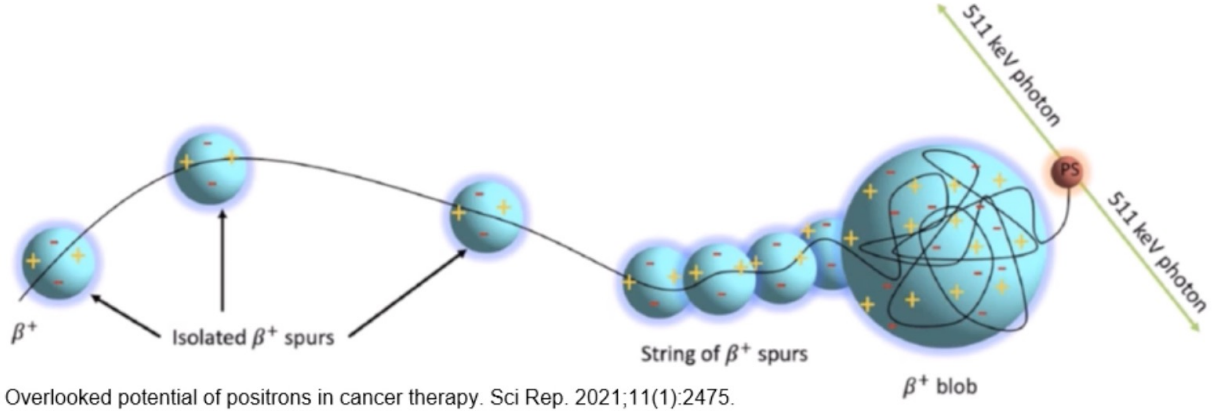
Auger e^-

- Examples: ^{111}In & ^{125}I have been used; ^{67}Ga, ^{99m}Tc & ^{123}I potential candidates



Positrons (β^+)* - ???

- Candidates: $^{61/64}Cu$, ^{89}Zr, ^{124}I



*Hioki T, Gholami YH, McKelvey KJ, Aslani A, Marquis H, Eslick EM, et al. Overlooked potential of positrons in cancer therapy. Sci Rep. 2021;11(1):2475.

D. Bailey, WC 2022

More Theranostic Terms

- **Targeted Molecular Radionuclide Therapy**
  - does not explicitly imply that it employs/requires imaging
- **Targeted Radiopharmaceutical Therapy**
  - not all treatments are due to radiolabeled molecules
- **Nuclear Theranostics**
  - is 'nuclear' referring to a cellular biological process?
- **Radiotheranostics**
  - is the pairing of radiolabeled diagnostic biomarkers with radiolabeled therapeutic agents that share a specific target in diseased cells or tissues
  - may involve radionuclides as radiotracers or radiolabeled biological molecules, e.g. radiopharmaceuticals.
  - diagnostic and therapeutic radiotheranostic pairs do not have to contain the same radionuclide

Clinical Applications for Cancer Control

- Unconjugated Radionuclides
  - I-131, Y-90, Ra-223, Sm 153…
- Radionuclide-Conjugated Cancer-Specific Vectors
  - Peptides
  - Small Molecules (PSMA, I-131 MIBG)
  - Antibodies
  - Nanoparticles

- **Current oncologic theranostic agents**
  - $^{123}I/^{131}I$ (NaI symporter; thyroid)
  - $^{111}In/^{90}Y$-ibritumomab (anti-CD20; lymphoma)
  - ^{18}F-NaF/^{99m}Tc-MDP; $^{223}RaCl_2$ (osteoblastic mets; mCRPC)*
  - ^{99m}Tc-MAA; ^{90}Y-microspheres (hyperperfusion; liver tumors)*
  - $^{123}I/^{131}I$-MIBG (norepinephrine transporter; pheochromocytoma, paraganglioma)
  - $^{68}Ga/^{64}Cu$-DOTATATE, ^{68}Ga-DOTATOC; ^{177}Lu-DOTATATE (SSTR+ neuroendocrine tumors)
- **Within near future**
  - ^{68}Ga*/^{18}F-PSMA*; ^{177}Lu-PSMA** (mCRPC)

(*FDA approved; ** FDA approval anticipated)

Adapted from H. Jadvar, 2021

- **In the horizon**
  - $^{225}Ac/^{227}Th$-PSMA (alpha RLT; mCRPC)
  - ^{68}Ga-pentixafor/^{177}Lu-, ^{90}Y-pentixather (chemokine receptor 4; multiple myeloma)
  - $^{68}Ga/^{177}Lu$-NeoB (GRPR; solid tumors)
  - $^{68}Ga/^{177}Lu$-FAPI (fibroblast activation protein; multiple cancers)
  - $^{89}Zr/^{177}Lu$-girentuximab (carbonic anhydrase IX; clear cell RCC)
  - $^{68}Ga/^{177}Lu$-FF58 (integrin $\alpha_3\beta_5$; GBM)
  - $^{18}F/^{131}I$-PARPi (DNA repair enzyme Poly-(ADP ribose) polymerase 1; multiple cancers)

Adapted from H. Jadvar, 2021

Potential / Essential Medical Physicist's Roles

- Search for New Radiotheranostic Agents
- Assess Methodologies of Radionuclide Cyclotron Production
- Design New Radionuclide Generators
- Suggest and Test Biomolecules' Radiolabelling Techniques
- Develop New Radionuclide Detectors and Imagers
- Standardize Activity Measurements
- Evaluate Radiopharmaceutical Biokinetic Distributions
- Examine Clinical DX and RX Radiopharmaceutical Protocols
- Determine Individualized Organ Doses
- Optimize Radiation Protection