Auger-Electron Emitters (AEE) for Targeted-Intercellular Therapy

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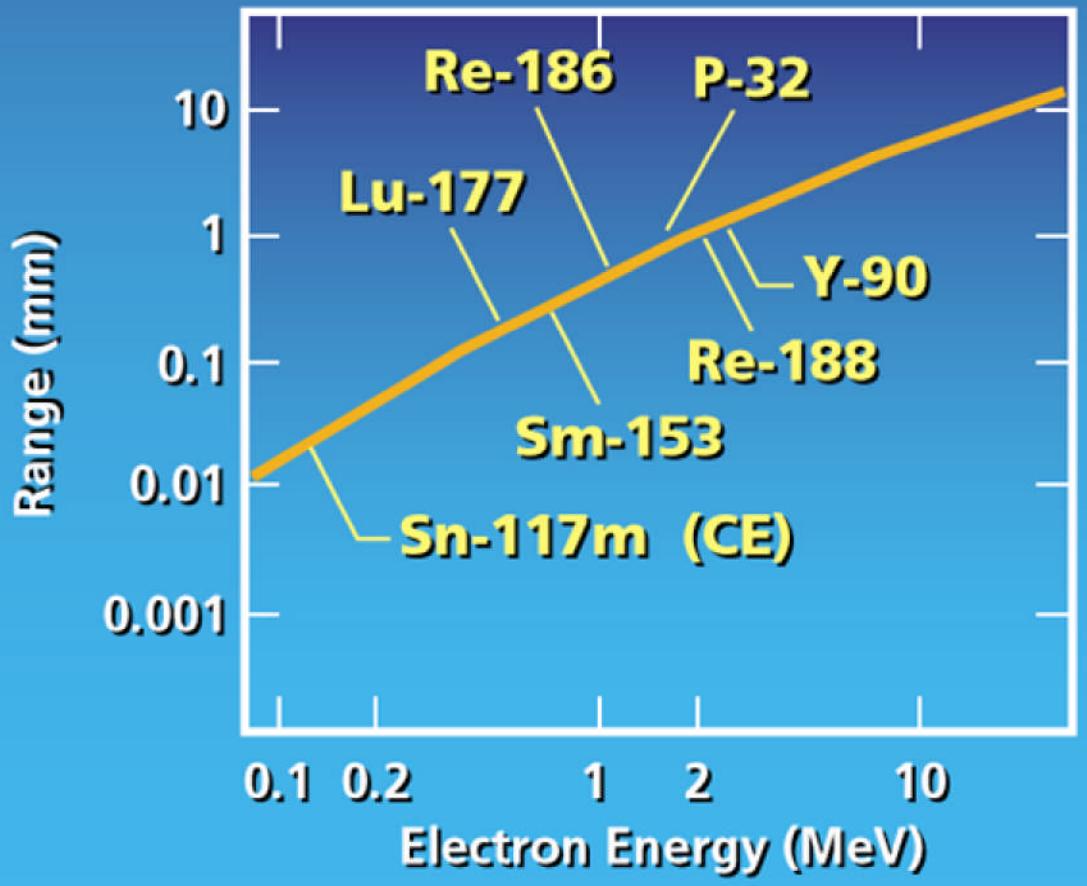
Rational

- The biological effects of AEE radionuclides can be as severe as those from α-emitting radionuclides – decay energy may be confined to a single cell
- Biological damage from AEE is highly dependent on the location of the decay site within the cell.
- Radio-Biological Equivalence (RBE) of AEE depends heavily on whether the nuclides are actually incorporated into cellular DNA or not
- Radiological risk from AEE may have been underestimated – lack of appropriate Dosimetry

Difficulties

- Decay energy from AEE are typically 1000 fold less than that from α-emitting radionuclides – consequently 1000 fold more AEE in required
- AEE need to be internalized into cells -- not very effective on cell surface
- Real Bottle-neck: selective *in-vivo* delivery of AEE to cells

Range of Electrons in Soft Tissue (Maximum Beta Energy)



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Depth of Radiation Penetration Required Depends Upon How Close We Can Approach the Cellular Target Regions

- **Beta particles** – up to 3 MeV – > 1 mm maximum – 50-250 cell diameters – "Cross Fire" Effect
- **Alpha particles** – 6-8 MeV – 5-10 cell diameters
- **Auger electrons** – < 10 angstrom range
- Nuclear targeting would be most effective

Estimated Energy Deposited from Auger Electrons in 5 mm Speroid

PLATINUM-195m	2000 eV
IODINE-125	1000 eV
INDIUM-111	450 eV

(FROM MARIANI AND BODEI, JNM, 2000)

Radionuclides Emitting Secondary Electrons for Intercellular Therapy

Radionuclide (Production)	Half-life	Emiss-ion	Q (keV)	<Ee> (keV)	Ne/Nt	Eγ keV (%)	Daughter Radioisotope
^{103}Ru (R)	30.4 d	β	763	41.7	?	497 (86)	^{103m}Rh (56.1 m)
^{103}Pd (R/A)	17.0 d	*EC*	546	42.7	7.4	357 (0.02)	^{103m}Rh (56.1 m)
^{103m}Rh (R)	56.1 m	*IT*	43	37.5	5.7	40 (0.07)	^{103}Rh (stable)
^{111}In (A)	2.8 d	*EC*	850	33.9	7.2	171 (90) +	^{111}Cd (stable)
^{123}I (A)	13.2 h	*EC*	1200	27.6	14	159 (83)	^{123}Te (10^{13} y)
^{125}I (R)	59.4 d	*EC*	178	17.9	23	35 (6.7)	^{125}Te (stable)
^{193m}Pt (R)	4.33 d	*IT*	150	130	22	135 (0.11)	^{193}Pt (50 y)
^{195m}Pt (R)	4.02 d	*IT*	260	175	36	99 (11)	^{195}Pt(stable)
^{195m}Hg (A)	1.73 d	*IT (54%)* *EC(46%)*	176 1520	140	15	262 (32) 560 (7.5)	^{195}Hg (9.5 h) ^{195}Au (183 d)
^{195}Hg (A)	9.5 h	*EC*	1520	61.3	23	780 (7.0)	^{195}Ag (185 d)
^{197m}Hg (R/A)	23.8	*IT(93%)* *EC (7%)*	299 600	214	30	140 (34)	^{197}Hg (2.67 d)
^{197}Hg (R/A)	2.67 d	*EC*	600	57	23	191 (0.6)	^{197}Au (stable)

Summary and Conclusions

- Broad interests in use of Auger-electron emitters for cancer therapy at cellular level
- Difficulty associated with delivery of required energy by AEE for killing a cell
- Very high specific activity is essential
- Mercury 197m and 197G are attractive candidates
- It is possible to produce high specific activity $^{197m\&g}Hg$ in reactor (10% hot atoms) and carrier-free in accelerator
- Chemistry of attaching Hg to biological molecules is well studied

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