

## AUGER-ELECTRON SPECTRA OF RADIONUCLIDES FOR THERAPY AND DIAGNOSTICS

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The present paper documents the calculation of radiation spectra and of radial dose distribution around a point source for 24 selected radionuclides. The radionuclides were ordered into three groups: Nuclides potentially useful for therapy by emission of Auger electrons:  $^{51}\text{Cr}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Ga}$ ,  $^{73}\text{Se}$ ,  $^{75}\text{Se}$ ,  $^{77}\text{Br}$ ,  $^{80\text{m}}\text{Br}$ ,  $^{94}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ,  $^{114\text{m}}\text{In}$ ,  $^{115\text{m}}\text{In}$ ,  $^{123}\text{I}$ ,  $^{124}\text{I}$ ,  $^{125}\text{I}$ ,  $^{167}\text{Tm}$ ,  $^{193\text{m}}\text{Pt}$ , and  $^{195\text{m}}\text{Pt}$ , nuclides potentially useful for therapy by  $\alpha$ -particles with additional emission of Auger electrons:  $^{212}\text{Bi}$ ,  $^{211}\text{At}$  and  $^{255}\text{Fm}$ , and nuclides potentially useful for electron Auger-therapy with simultaneous PET diagnosis:  $^{73}\text{Se}$ ,  $^{94}\text{Tc}$  and  $^{124}\text{I}$ . The calculations imply strongly the development of labelled DNA-seeking compounds useful as carrier for the Auger- and Coster-Kronig electron-emitting radionuclides.

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In both diagnostic and therapeutic nuclear medicine a large number of radionuclides is regularly used; other nuclides are scope if intense research. In all applications of radiopharmaceuticals, however, an exact knowledge of their dosimetry is mandatory: in diagnostics, it must be proven that radiation dose to patients really is a negligible effect, and in therapy, successful treatment is strongly dependent on the administered dose under greatest possible saving of the healthy tissue. Since the nature of emitted radiation varies with nuclides, a general calculation mode of radiation dose is difficult if not impossible; the relation between radiation and damage is generally described by models. Based on such models, the strategy of treatment can be tailored on distinct needs.

To date, radiation dosimetry of nuclear medical applications has been estimated generally by a strategy of dose effects in an organ, i.e. dimensions of at least some mil-

limetres have been assumed, as well as uniform distribution of radiopharmaceutical in a corresponding volume. This 'macrodosimetric' concept has been outlined in detail by the 'Medical Internal Radiation Dose' Committee (MIRD) (1, 2), by the (U.S.) Society of Nuclear Medicine and by the International Commission of Radiation Protection (ICRP) (3) and in many treatments it meets the demands on accuracy of dose data in a satisfying way.

In order to protect normal tissue from irradiation by radionuclides, recent research emphasized sub-cellular localisation of sources of high LET radiation with very short ranges in tissue (4–6). In this consensus, the potential of therapeutically useful nuclides decaying by electron capture or by internal conversion have been considered. They decay emitting Auger and Coster-Kronig electrons as a result of electron transitions between different atomic shells. The extreme radiotoxicity of Auger electron emitters has been well documented by Rao et al. (7) and is attributed to the highly localised energy deposition in the immediate vicinity of the decay site (8–10).

Attempts in creating an  $\alpha$ -particle dosimetry of  $^{211}\text{At}$  have been performed but without considering its emission of Auger electrons (11–13). Recently, some papers have been published with similar attitude (14, 15).

For direct damage of DNA by attached radionuclides, mainly the very low-energy N- and O-shell Auger electrons

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Received 23 October 1995.

Accepted 30 July 1996.

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Paper presented at the Third International Symposium on Biophysical Aspects of Auger Processes, August 24–25, 1995, Lund, Sweden.

are responsible, since they deposit their energy over just a few tens of nanometers, or less. On the other hand, exact data about emission of Auger electrons from outer shells of radioactive atoms are not yet exactly known.

The present paper documents the calculation of radiation spectra and radial dose distributions of selected radionuclides decaying under emission of Auger electrons. The radionuclides are ordered into three groups:

- 1) Nuclides useful potentially for tumour therapy by emission of Auger electrons:  $^{51}\text{Cr}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Ga}$ ,  $^{73}\text{Se}$ ,  $^{75}\text{Se}$ ,  $^{77}\text{Br}$ ,  $^{80\text{m}}\text{Br}$ ,  $^{94}\text{Tc}$ ,  $^{99\text{m}}\text{Tc}$ ,  $^{114\text{m}}\text{In}$ ,  $^{115\text{m}}\text{In}$ ,  $^{123}\text{I}$ ,  $^{124}\text{I}$ ,  $^{125}\text{I}$ ,  $^{167}\text{Tm}$ ,  $^{193\text{m}}\text{Pt}$ , and  $^{195\text{m}}\text{Pt}$ ,
- 2) Nuclides potentially useful for therapy by  $\alpha$ -particles with additional emission of Auger electrons:  $^{212}\text{Bi}$ ,  $^{211}\text{At}$  and  $^{255}\text{Fm}$ ,
- 3) Nuclides potentially useful for electron Auger-therapy with simultaneous PET diagnosis:  $^{73}\text{Se}$ ,  $^{94}\text{Tc}$  and  $^{124}\text{I}$ .

Table 1 specifies decay modes and half-lives of considered radionuclides. Also it gives the average number of Auger and Coster-Kronig electrons emitted per decay as calculated using IMRDEC.

The proposed list of radionuclides is of course incomplete and may be extended. It represents rather a compromise between proposed importance emission of rate of Auger electrons and knowledge of both labelling techniques and biochemical behaviour of the labelled compound. In most cases, this basic scientific knowledge has been elaborated for use in a diagnostic nuclear medicine.

**Table 1**

*Decay modes and half-lives (Abbreviations: IC means internal conversion and EC electron capture mode)*

Nuclide	Decay mode	Half life
$^{51}\text{Cr}$	IC + EC	2.77 d
$^{64}\text{Cu}$	EC + $\beta^-$ + $\beta^+$	12.7 h
$^{67}\text{Ga}$	IC + EC	3.36 d
$^{73}\text{Se}$	EC + $\beta^+$	39.8 m
$^{75}\text{Se}$	IC + EC	1.20 d
$^{77}\text{Br}$	IC	2.38 d
$^{80\text{m}}\text{Br}$	IC + EC + $\beta^-$ + $\beta^+$	4.42 h
$^{94}\text{Tc}$	IC + EC + $\beta^+$	4.42 h
$^{99\text{m}}\text{Tc}$	IC + $\beta^-$	6.01 h
$^{114\text{m}}\text{In}$	IC + EC	4.95 d
$^{115\text{m}}\text{In}$	IC + $\beta^-$	4.49 h
$^{123}\text{I}$	EC	13.2 h
$^{124}\text{I}$	EC + $\beta^+$	4.18 d
$^{125}\text{I}$	IC + EC	60.1 d
$^{167}\text{Tm}$	IC + EC	9.25 d
$^{193\text{m}}\text{Pt}$	IC	4.33 d
$^{195\text{m}}\text{Pt}$	IC	4.02 d
$^{212}\text{Bi}$	IC + $\beta^-$ + $\alpha$	1.01 h
$^{211}\text{At}$	IC + EC + $\alpha$	7.21 h
$^{255}\text{Fm}$	IC + $\alpha$	5.30 h

The investigated nuclides are either metallic complexing agents or halogens respectively. The metallic nuclides can be used for labelling proteins, particularly monoclonal antibodies which are discussed for radioimmunotherapy (16). Monoclonal antibodies, however, generally do not penetrate the cell membrane; consequently the short-ranged Auger electrons of their labels do not reach the DNA. Thus, for therapy with Auger emitters, monoclonal antibodies should be of limited value. On the other hand, there are other proteins penetrating cell membranes (EGF, TGF etc., for example) but to our knowledge, those have not yet been labelled with Auger emitters. This approach, however, could be an interesting one.

Among the metallic Auger emitters, because of their high emission rates, the platinum isotopes  $^{193\text{m}}\text{Pt}$  and  $^{195\text{m}}\text{Pt}$  could be of valuable interest. Both nuclides have been applied: for diagnostic purposes the chemotherapeutic cisplatin and some of its derivatives have been labelled with  $^{193\text{m}}\text{Pt}$  and  $^{195\text{m}}\text{Pt}$  (17–20). The authors, however, unanimously claimed the high enrichment of radioactive platinum in kidneys and the urinary tract which should prevent its therapeutic application without further research.

The exotic radionuclide 20.1 h  $^{255}\text{Fm}$  has been proposed (21) because of its convenient half-life and its  $\alpha$ -particle emission. This nuclide, however, decays (as other  $\alpha$ -particle emitting heavy radionuclides) to long-lived  $\alpha$ -particle emitting daughter nuclides which would act as potential long-lived radiation sources in the body. This, together with its extremely low availability, should prevent the use of  $^{255}\text{Fm}$  for therapeutic application.

From point of view of clinical tumour therapeutics,  $^{211}\text{At}$  is a very interesting radionuclide. Its high-LET radiotoxicity is well documented (22, 23). It could be caused mainly by formation of radicals along the  $\alpha$ -particle track. It would be of high interest to label DNA itself or via an intercalator, with  $^{211}\text{At}$ , in order to find out the enhancement of its  $\alpha$ -particle radiotoxicity by activity of its Auger electrons. It might be expected that, by means of both kinds of radiation, only an extremely low amount of  $^{211}\text{At}$  may be necessary to kill the tumour cells, and that the healthy tissue might be saved mainly by the low concentration of  $^{211}\text{At}$ . So far, no results have been obtained yet in order to clarify the mechanism of radiotoxicity of  $^{211}\text{At}$ . Therefore, we performed some calculations of the radial dose distribution of  $^{211}\text{At}$  with and without consideration of its Auger and Coster-Kronig electrons.

#### Emission spectra

Calculations of the emission spectra were calculated using the computer program IMRDEC. A short description of this program is given by Stepanek (unpublished study). For a detailed description see (24) and especially (25).

Table 2

Average Auger and Coster-Kronig electron spectra per Decay: Condensed phase

Process	Chromium-51		Copper-64		Gallium-67		Selenium-73		Selenium
	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)
KLL	$4.75 \cdot 10^{+3}$	$5.18 \cdot 10^{-1}$	$6.99 \cdot 10^{+3}$	$1.71 \cdot 10^{-1}$	$8.00 \cdot 10^{+3}$	$4.84 \cdot 10^{-1}$	$9.62 \cdot 10^{+3}$	$6.63 \cdot 10^{-2}$	$9.63 \cdot 10^{+3}$
KLX	$5.29 \cdot 10^{+3}$	$1.20 \cdot 10^{-1}$	$7.88 \cdot 10^{+3}$	$4.23 \cdot 10^{-2}$	$9.05 \cdot 10^{+3}$	$1.29 \cdot 10^{-1}$	$1.10 \cdot 10^{+4}$	$2.03 \cdot 10^{-2}$	$1.10 \cdot 10^{+4}$
KXY	$5.84 \cdot 10^{+3}$	$7.46 \cdot 10^{-3}$	$8.77 \cdot 10^{+3}$	$2.94 \cdot 10^{-3}$	$1.01 \cdot 10^{+4}$	$9.29 \cdot 10^{-3}$	$1.23 \cdot 10^{+4}$	$1.59 \cdot 10^{-3}$	$1.23 \cdot 10^{+4}$
LLX	$6.14 \cdot 10^{+1}$	$1.73 \cdot 10^{-1}$	$9.12 \cdot 10^{+1}$	$1.02 \cdot 10^{-1}$	$9.50 \cdot 10^{+1}$	$3.00 \cdot 10^{-1}$	$8.14 \cdot 10^{+1}$	$6.18 \cdot 10^{-2}$	$9.55 \cdot 10^{+1}$
LMM	$5.04 \cdot 10^{+2}$	$1.45 \cdot 10^{+0}$	$8.58 \cdot 10^{+2}$	$5.66 \cdot 10^{-1}$	$1.01 \cdot 10^{+3}$	$1.73 \cdot 10^{+0}$	$1.24 \cdot 10^{+3}$	$7.21 \cdot 10^{-1}$	$1.24 \cdot 10^{+3}$
LMX	$3.60 \cdot 10^{+2}$	$2.30 \cdot 10^{-2}$	$8.99 \cdot 10^{+2}$	$2.15 \cdot 10^{-3}$	$1.05 \cdot 10^{+3}$	$2.76 \cdot 10^{-2}$	$1.31 \cdot 10^{+3}$	$3.40 \cdot 10^{-2}$	$1.32 \cdot 10^{+3}$
LXY	-	-	-	-	$1.16 \cdot 10^{+3}$	$1.48 \cdot 10^{-4}$	$1.43 \cdot 10^{+3}$	$6.04 \cdot 10^{-4}$	$1.44 \cdot 10^{+3}$
MMX	$3.60 \cdot 10^{+1}$	$2.30 \cdot 10^{+0}$	$5.69 \cdot 10^{+1}$	$7.68 \cdot 10^{-1}$	$5.48 \cdot 10^{+1}$	$2.13 \cdot 10^{+0}$	$5.46 \cdot 10^{+1}$	$8.10 \cdot 10^{-1}$	$5.58 \cdot 10^{+1}$
MXY	-	-	-	-	$1.15 \cdot 10^{+1}$	$2.22 \cdot 10^{+0}$	$3.31 \cdot 10^{+1}$	$2.16 \cdot 10^{+0}$	$3.51 \cdot 10^{+1}$
Total	$3.97 \cdot 10^{+3}$	$4.68 \cdot 10^{+0}$	$2.09 \cdot 10^{+3}$	$1.65 \cdot 10^{+0}$	$7.07 \cdot 10^{+3}$	$7.03 \cdot 10^{+0}$	$1.94 \cdot 10^{+3}$	$3.88 \cdot 10^{+0}$	$5.94 \cdot 10^{+3}$
Process	Bromine-77		Bromine-80m		Technicium-94		Technicium-99m		Indium
	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)
KLL	$1.02 \cdot 10^{+4}$	$1.90 \cdot 10^{-1}$	$1.02 \cdot 10^{+4}$	$3.62 \cdot 10^{-1}$	$1.54 \cdot 10^{+4}$	$1.21 \cdot 10^{-1}$	$1.54 \cdot 10^{+4}$	$1.50 \cdot 10^{-2}$	$2.01 \cdot 10^{+4}$
KLX	$1.16 \cdot 10^{+4}$	$5.91 \cdot 10^{-2}$	$1.16 \cdot 10^{+4}$	$1.17 \cdot 10^{-1}$	$1.78 \cdot 10^{+4}$	$4.62 \cdot 10^{-2}$	$1.78 \cdot 10^{+4}$	$5.17 \cdot 10^{-3}$	$2.34 \cdot 10^{+4}$
KXY	$1.31 \cdot 10^{+4}$	$4.62 \cdot 10^{-3}$	$1.31 \cdot 10^{+4}$	$9.57 \cdot 10^{-3}$	$2.02 \cdot 10^{+4}$	$4.25 \cdot 10^{-3}$	$2.02 \cdot 10^{+4}$	$4.32 \cdot 10^{-4}$	$2.67 \cdot 10^{+4}$
LLX	$8.97 \cdot 10^{+1}$	$1.49 \cdot 10^{-1}$	$9.27 \cdot 10^{+1}$	$3.19 \cdot 10^{-1}$	$1.07 \cdot 10^{+2}$	$1.66 \cdot 10^{-1}$	$1.06 \cdot 10^{+2}$	$2.10 \cdot 10^{-2}$	$2.29 \cdot 10^{+2}$
LMM	$1.32 \cdot 10^{+3}$	$8.89 \cdot 10^{-1}$	$1.32 \cdot 10^{+3}$	$1.70 \cdot 10^{+0}$	$2.06 \cdot 10^{+3}$	$7.41 \cdot 10^{-1}$	$2.07 \cdot 10^{+3}$	$9.01 \cdot 10^{-2}$	$2.74 \cdot 10^{+3}$
LMX	$1.41 \cdot 10^{+3}$	$5.45 \cdot 10^{-2}$	$1.41 \cdot 10^{+3}$	$1.10 \cdot 10^{-1}$	$2.33 \cdot 10^{+3}$	$1.19 \cdot 10^{-1}$	$2.34 \cdot 10^{+3}$	$1.44 \cdot 10^{-2}$	$3.21 \cdot 10^{+3}$
LXY	$1.55 \cdot 10^{+3}$	$1.30 \cdot 10^{-3}$	$1.55 \cdot 10^{+3}$	$2.75 \cdot 10^{-3}$	$2.64 \cdot 10^{+3}$	$5.48 \cdot 10^{-3}$	$2.64 \cdot 10^{+3}$	$6.82 \cdot 10^{-4}$	$3.71 \cdot 10^{+3}$
MMX	$6.00 \cdot 10^{+1}$	$1.01 \cdot 10^{+0}$	$6.25 \cdot 10^{+1}$	$1.96 \cdot 10^{+0}$	$1.10 \cdot 10^{+2}$	$7.72 \cdot 10^{-1}$	$1.14 \cdot 10^{+2}$	$8.69 \cdot 10^{-1}$	$1.28 \cdot 10^{+2}$
MXY	$4.53 \cdot 10^{+1}$	$2.61 \cdot 10^{+0}$	$4.52 \cdot 10^{+1}$	$4.96 \cdot 10^{+0}$	$2.09 \cdot 10^{+2}$	$1.90 \cdot 10^{+0}$	$2.12 \cdot 10^{+2}$	$1.08 \cdot 10^{+0}$	$3.73 \cdot 10^{+2}$
NNX	-	-	-	-	$2.90 \cdot 10^{+1}$	$2.55 \cdot 10^{+0}$	$2.97 \cdot 10^{+1}$	$2.57 \cdot 10^{+0}$	$3.38 \cdot 10^{+1}$
NXY	-	-	-	-	-	-	-	-	$9.15 \cdot 10^{+0}$
Total	$4.13 \cdot 10^{+3}$	$4.96 \cdot 10^{+0}$	$7.97 \cdot 10^{+3}$	$9.54 \cdot 10^{+0}$	$5.17 \cdot 10^{+3}$	$6.42 \cdot 10^{+0}$	$9.60 \cdot 10^{+2}$	$4.67 \cdot 10^{+0}$	$4.00 \cdot 10^{+3}$

The program IMRDEC reads the decay schemes from the Evaluated Nuclear Structure Data File (ENSDF) (26). The atomic data as well as the atomic relaxation probabilities are obtained reading the Evaluated Atomic Data Library (EADL) (27).

Tables 2 and 3 show the detailed Auger and Coster-Kronig spectra of selected radionuclides. They were calculated considering the complete decay chains down to the nuclide whose half-life is considerably longer as that of the mother radionuclide.  $^{80m}\text{Br}$ ,  $^{212}\text{Bi}$  and  $^{211}\text{At}$  were considered to be in equilibrium with their short-lived daughter nuclides, i.e.  $^{80m}\text{Br}$  with  $17.6\text{ m }^{80}\text{Br}$ ,  $^{212}\text{Bi}$  with  $3.1\text{ m }^{208}\text{Tl}$  and  $^{211}\text{At}$  with  $0.52\text{ s }^{211}\text{Po}$ .  $^{213}\text{Bi}$  was calculated in equilibrium with its daughter nuclides  $2.2\text{ m }^{209}\text{Tl}$  and  $4.2\text{ }\mu\text{s }^{213}\text{Po}$ . Because of its expected slow retention from body, its longer-lived daughter nuclide  $3.25\text{ h }^{209}\text{Pb}$  has also been added considering the same decay intensity as that of  $^{213}\text{Bi}$ .

With exception of  $^{64}\text{Cu}$ , the investigated nuclides emit 5 or more conversion and Auger and Coster-Kronig electrons which can principally impair cell proliferation, mostly by double strand breaks. If it can be managed to place high selectively these Auger emitters in close proximity to the DNA of tumour cell, a great potential for radionuclide therapy becomes accessible.

Tables show that a considerable amount of electrons with energies below 200 eV are emitted which have very short stopping range in tissue. Therefore, when these nuclides are incorporated into DNA, then the emitted Auger and Coster-Kronig electrons strongly ionise the nearest space around the DNA and produce free radicals. The emitted electrons are able to ionize directly the DNA and thus to produce primary single and double DNA strand breaks (physical stage) and the generated radicals can diffuse and react amongst themselves and with subunits of DNA which leads to secondary single and DNA strand breaks (28) (chemical stage).

#### Radial energy and dose distributions

The radial dose distributions were calculated using the IMR version of the Monte Carlo code GEANT (29, 30). The calculations were performed in a sphere of 1 cm radius under the assumption that the radionuclide is placed in the centre of the sphere. Soft tissue has been assumed to be the tracking material. All Monte Carlo calculations were performed down to 10 eV considering  $10^5$  decays (histories).

The IMR version of the code GEANT performs particle tracking accurate in nanometer range. It uses the photon

**Table 3**  
Average Auger and Coster-Kronig electron spectra per decay; Condensed phase.

Process	Indium-115m		Iodine-123		Iodine-124		Iodine-125		Thulium	
	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)
KLL	$2.01 \cdot 10^{+4}$	$3.88 \cdot 10^{-2}$	$2.36 \cdot 10^{+4}$	$7.45 \cdot 10^{-2}$	$2.36 \cdot 10^{+4}$	$4.94 \cdot 10^{-2}$	$2.36 \cdot 10^{+4}$	$1.18 \cdot 10^{-1}$	$4.07 \cdot 10^{+4}$	$3.26 \cdot 10^{-2}$
KLX	$2.34 \cdot 10^{+4}$	$1.64 \cdot 10^{-2}$	$2.76 \cdot 10^{+4}$	$3.37 \cdot 10^{-2}$	$2.76 \cdot 10^{+4}$	$2.23 \cdot 10^{-2}$	$2.76 \cdot 10^{+4}$	$5.37 \cdot 10^{-2}$	$4.84 \cdot 10^4$	$1.70 \cdot 10^{-2}$
KXY	$2.67 \cdot 10^{+4}$	$1.66 \cdot 10^{-3}$	$3.16 \cdot 10^{+4}$	$3.65 \cdot 10^{-3}$	$3.16 \cdot 10^{+4}$	$2.41 \cdot 10^{-3}$	$3.16 \cdot 10^{+4}$	$5.84 \cdot 10^{-3}$	$5.61 \cdot 10^{+4}$	$2.13 \cdot 10^{-3}$
LLX	$2.65 \cdot 10^{+2}$	$6.41 \cdot 10^{-2}$	$3.10 \cdot 10^{+2}$	$1.44 \cdot 10^{-1}$	$3.10 \cdot 10^{+2}$	$9.69 \cdot 10^{-2}$	$3.15 \cdot 10^{+2}$	$2.52 \cdot 10^{-1}$	$6.71 \cdot 10^{+2}$	$2.40 \cdot 10^{-1}$
LMM	$2.74 \cdot 10^{+3}$	$3.35 \cdot 10^{-1}$	$3.21 \cdot 10^{+3}$	$7.17 \cdot 10^{-1}$	$3.21 \cdot 10^{+3}$	$4.75 \cdot 10^{-1}$	$3.22 \cdot 10^{+3}$	$1.18 \cdot 10^{+0}$	$5.69 \cdot 10^{+3}$	$8.02 \cdot 10^{-1}$
LMX	$3.22 \cdot 10^{+3}$	$8.26 \cdot 10^{-2}$	$3.84 \cdot 10^{+3}$	$2.15 \cdot 10^{-1}$	$3.84 \cdot 10^{+3}$	$1.42 \cdot 10^{-1}$	$3.85 \cdot 10^{+3}$	$3.55 \cdot 10^{-1}$	$7.12 \cdot 10^{+3}$	$2.93 \cdot 10^{-1}$
LXY	$3.72 \cdot 10^{+3}$	$5.32 \cdot 10^{-3}$	$4.50 \cdot 10^{+3}$	$1.60 \cdot 10^{-2}$	$4.50 \cdot 10^{+3}$	$1.05 \cdot 10^{-2}$	$4.51 \cdot 10^{+3}$	$2.64 \cdot 10^{-2}$	$8.59 \cdot 10^{+3}$	$2.71 \cdot 10^{-2}$
MMX	$1.26 \cdot 10^{+2}$	$3.72 \cdot 10^{-1}$	$1.20 \cdot 10^{+2}$	$8.21 \cdot 10^{-1}$	$1.20 \cdot 10^{+2}$	$5.46 \cdot 10^{-1}$	$1.20 \cdot 10^{+2}$	$1.36 \cdot 10^{+0}$	$2.53 \cdot 10^{+2}$	$1.07 \cdot 10^{+0}$
MXY	$3.73 \cdot 10^{+2}$	$8.61 \cdot 10^{-1}$	$4.84 \cdot 10^{+2}$	$1.93 \cdot 10^{+0}$	$4.84 \cdot 10^{+2}$	$1.28 \cdot 10^{+0}$	$4.84 \cdot 10^{+2}$	$3.17 \cdot 10^{+0}$	$1.21 \cdot 10^{+3}$	$2.52 \cdot 10^{+0}$
NNX	$3.36 \cdot 10^{+1}$	$1.19 \cdot 10^{+1}$	$2.62 \cdot 10^{+1}$	$2.23 \cdot 10^{+0}$	$2.61 \cdot 10^{+1}$	$1.48 \cdot 10^{+0}$	$2.63 \cdot 10^{+1}$	$3.68 \cdot 10^{+0}$	$1.47 \cdot 10^{+2}$	$6.11 \cdot 10^{+0}$
NXY	$8.48 \cdot 10^{+0}$	$2.08 \cdot 10^{+0}$	$2.93 \cdot 10^{+1}$	$6.47 \cdot 10^{+0}$	$3.15 \cdot 10^{+1}$	$4.50 \cdot 10^{+0}$	$2.94 \cdot 10^{+1}$	$1.07 \cdot 10^{+1}$	$2.25 \cdot 10^{+2}$	$2.32 \cdot 10^{-1}$
Total	$2.85 \cdot 10^{+3}$	$5.04 \cdot 10^{+0}$	$7.33 \cdot 10^{+3}$	$1.26 \cdot 10^{+1}$	$4.87 \cdot 10^{+3}$	$8.60 \cdot 10^{+0}$	$1.19 \cdot 10^{+4}$	$2.10 \cdot 10^{+1}$	$1.36 \cdot 10^{+4}$	$1.14 \cdot 10^{+1}$
Process	Platinum-193m		Platinum-195m		Bismuth-212		Astatine-211		Fermium-255	
	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)	Av. En. (eV)	Yield (eV)
KLL	$5.26 \cdot 10^{+4}$	$4.21 \cdot 10^{-3}$	$5.32 \cdot 10^{+4}$	$1.39 \cdot 10^{-2}$	$5.74 \cdot 10^{+4}$	$1.54 \cdot 10^{-3}$	$6.35 \cdot 10^{+4}$	$9.74 \cdot 10^{-3}$	$9.08 \cdot 10^{+4}$	$8.82 \cdot 10^{-6}$
KLX	$6.32 \cdot 10^{+4}$	$2.37 \cdot 10^{-3}$	$6.35 \cdot 10^{+4}$	$9.06 \cdot 10^{-3}$	$6.90 \cdot 10^{+4}$	$8.45 \cdot 10^{-4}$	$7.67 \cdot 10^4$	$5.49 \cdot 10^{-3}$	$1.12 \cdot 10^{+5}$	$5.60 \cdot 10^{-6}$
KXY	$7.37 \cdot 10^{+4}$	$1.08 \cdot 10^{-3}$	$7.39 \cdot 10^{+4}$	$1.44 \cdot 10^{-3}$	$8.07 \cdot 10^{+4}$	$1.11 \cdot 10^{-4}$	$8.68 \cdot 10^{+4}$	$7.47 \cdot 10^{-4}$	$1.32 \cdot 10^{+5}$	$8.67 \cdot 10^{-7}$
LLX	$9.81 \cdot 10^{+2}$	$4.18 \cdot 10^{-2}$	$5.80 \cdot 10^{+2}$	$7.12 \cdot 10^{-1}$	$8.47 \cdot 10^{+2}$	$1.44 \cdot 10^{-1}$	$1.15 \cdot 10^{+3}$	$9.09 \cdot 10^{-2}$	$2.74 \cdot 10^{+3}$	$2.29 \cdot 10^{-1}$
LMM	$7.08 \cdot 10^{+3}$	$4.94 \cdot 10^{-1}$	$7.26 \cdot 10^{+3}$	$9.05 \cdot 10^{-1}$	$8.22 \cdot 10^{+3}$	$1.05 \cdot 10^{-1}$	$8.67 \cdot 10^{+3}$	$1.75 \cdot 10^{-1}$	$1.19 \cdot 10^{+4}$	$3.35 \cdot 10^{-1}$
LMX	$9.10 \cdot 10^{+3}$	$1.99 \cdot 10^{-1}$	$9.29 \cdot 10^{+3}$	$4.08 \cdot 10^{-1}$	$1.07 \cdot 10^{+4}$	$4.71 \cdot 10^{-2}$	$1.13 \cdot 10^{+4}$	$8.23 \cdot 10^{-2}$	$1.61 \cdot 10^{+4}$	$1.91 \cdot 10^{-1}$
LXY	$1.12 \cdot 10^{+4}$	$1.94 \cdot 10^{-2}$	$1.14 \cdot 10^{+4}$	$4.48 \cdot 10^{-2}$	$1.31 \cdot 10^{+4}$	$5.08 \cdot 10^{-3}$	$1.40 \cdot 10^{+4}$	$9.19 \cdot 10^{-3}$	$2.03 \cdot 10^{+4}$	$2.54 \cdot 10^{-2}$
MMX	$3.73 \cdot 10^{+2}$	$7.22 \cdot 10^{-1}$	$3.71 \cdot 10^{+2}$	$1.35 \cdot 10^{+0}$	$4.39 \cdot 10^{+2}$	$1.89 \cdot 10^{-1}$	$4.42 \cdot 10^{+2}$	$2.77 \cdot 10^{-1}$	$7.56 \cdot 10^{+2}$	$1.22 \cdot 10^{+0}$
MXY	$1.73 \cdot 10^{+3}$	$1.85 \cdot 10^{+0}$	$1.73 \cdot 10^{+3}$	$3.68 \cdot 10^{+0}$	$1.97 \cdot 10^{+3}$	$4.73 \cdot 10^{-1}$	$2.11 \cdot 10^{+3}$	$7.20 \cdot 10^{-1}$	$3.11 \cdot 10^{+3}$	$2.13 \cdot 10^{+0}$
NNX	$1.76 \cdot 10^{+2}$	$4.65 \cdot 10^{+0}$	$1.78 \cdot 10^{+2}$	$6.36 \cdot 10^{+0}$	$1.75 \cdot 10^{+2}$	$7.84 \cdot 10^{-1}$	$1.78 \cdot 10^{+2}$	$1.13 \cdot 10^{+0}$	$2.06 \cdot 10^{+2}$	$3.14 \cdot 10^{+0}$
NXY	$6.48 \cdot 10^{+1}$	$7.73 \cdot 10^{+0}$	$6.99 \cdot 10^{+1}$	$1.18 \cdot 10^{+1}$	$8.88 \cdot 10^{+1}$	$1.48 \cdot 10^{+0}$	$1.09 \cdot 10^{+2}$	$2.08 \cdot 10^{+0}$	$4.39 \cdot 10^{+2}$	$5.48 \cdot 10^{+0}$
OOX	$3.99 \cdot 10^{+1}$	$4.56 \cdot 10^{+0}$	$4.20 \cdot 10^{+1}$	$6.20 \cdot 10^{+0}$	$4.11 \cdot 10^{+0}$	$1.06 \cdot 10^{+0}$	$3.84 \cdot 10^{+1}$	$1.63 \cdot 10^{+0}$	$1.32 \cdot 10^{+2}$	$4.61 \cdot 10^{+0}$
OXY	—	—	—	—	$1.18 \cdot 10^{+2}$	$2.06 \cdot 10^{-3}$	$1.27 \cdot 10^{+2}$	$5.24 \cdot 10^{-3}$	$2.45 \cdot 10^{+2}$	$1.91 \cdot 10^{-2}$
Total	$1.09 \cdot 10^{+4}$	$2.03 \cdot 10^{+1}$	$2.18 \cdot 10^{+4}$	$3.15 \cdot 10^{+1}$	$3.04 \cdot 10^{+3}$	$4.30 \cdot 10^{+0}$	$5.92 \cdot 10^{+3}$	$6.21 \cdot 10^{+0}$	$1.94 \cdot 10^{+4}$	$1.74 \cdot 10^{+1}$

and electron libraries EPDL (Evaluated Photon Data Library) (31) and EEDL (Evaluated Electron Data Library) (32) which were provided by Lawrence Livermore National Laboratory. These files contain cross-sections for elements from  $Z = 1$  to 100 in the energy range from 10 eV to 100 GeV (see (29) for more details). Also used is the own water-vapour library for electrons, which consists of data in the energy range from 1 eV to 100 GeV. Besides the cross-sections for the most important processes, they contain the cross-sections for ionisation by photon or electron for each atomic subshell.

Based on calculated dose distributions, the fractions of the ratios of the average doses to that in the first 1 nm were determined in three radial zones:  $R \leq 10$  nm,  $10 \text{ nm} < R \leq 100 \text{ nm}$  and  $100 \text{ nm} < R \leq 1 \mu\text{m}$ .

The results are given in Table 4. It can be seen that all dose ratios decrease very strongly with increasing radius. Their shape is closed to the geometrical dilution due to the

spherical geometry. The decrease is so high that it can be assumed that it would be large enough even if we would consider other geometries, such as a line source in cylindrical geometry, for example.

The values of  $^{212}\text{Bi}^*$ ,  $^{211}\text{At}^*$  and  $^{255}\text{Fm}^*$  were calculated also without the contribution of Auger and Coster-Kronig electrons. It can be seen that without these electrons the radial decrease of the dose is by a factor of about 10 smaller.

These results indicate that, from the physics point of view, all considered radionuclides are well useful to be bound onto the DNA.

To conclude, by means of our calculation method, the Auger spectra and radial dose distributions around a point source of selected therapeutically useful nuclides have been calculated. The results stress the development of labelled DNA-seeking compounds useful as carrier for the Auger and Coster-Kronig electron-emitting radionuclides.

Table 4

Dose and spatial distribution of the ratio of dose normalised to the average dose in sphere or radius 10 nm

Nuclide	Equilibrium dose (Gy-hour/nuclide)	Average dose (Gy-hour/nuclide) R ≤ 10 nm	Dose ratio	
			10 nm < R ≤ 100 nm	100 nm < R ≤ 1 μm
<sup>51</sup> Cr	6.32 · 10 <sup>-19</sup>	2.10 · 10 <sup>-1</sup>	4.20 · 10 <sup>-3</sup>	1.61 · 10 <sup>-7</sup>
<sup>64</sup> Cu	3.70 · 10 <sup>-16</sup>	3.65 · 10 <sup>+2</sup>	2.45 · 10 <sup>-03</sup>	1.46 · 10 <sup>-5</sup>
<sup>67</sup> Ga	3.16 · 10 <sup>-17</sup>	1.25 · 10 <sup>+2</sup>	3.26 · 10 <sup>-03</sup>	1.18 · 10 <sup>-5</sup>
<sup>73</sup> Se	1.41 · 10 <sup>-14</sup>	1.67 · 10 <sup>-4</sup>	2.72 · 10 <sup>-3</sup>	1.12 · 10 <sup>-5</sup>
<sup>75</sup> Se	1.24 · 10 <sup>-18</sup>	4.28 · 10 <sup>+0</sup>	2.59 · 10 <sup>-3</sup>	1.07 · 10 <sup>-5</sup>
<sup>77</sup> Br	3.76 · 10 <sup>-14</sup>	2.03 · 10 <sup>+5</sup>	2.10 · 10 <sup>-3</sup>	7.69 · 10 <sup>-6</sup>
<sup>80m</sup> Br	8.53 · 10 <sup>-15</sup>	3.41 · 10 <sup>-4</sup>	3.02 · 10 <sup>-3</sup>	2.96 · 10 <sup>-6</sup>
<sup>94</sup> Tc	6.18 · 10 <sup>-15</sup>	3.34 · 10 <sup>-3</sup>	3.13 · 10 <sup>-3</sup>	8.13 · 10 <sup>-6</sup>
<sup>99m</sup> Tc	3.87 · 10 <sup>-15</sup>	5.24 · 10 <sup>-3</sup>	1.88 · 10 <sup>-3</sup>	4.94 · 10 <sup>-6</sup>
<sup>114m</sup> In	4.45 · 10 <sup>-18</sup>	1.69 · 10 <sup>+1</sup>	3.01 · 10 <sup>-3</sup>	2.26 · 10 <sup>-6</sup>
<sup>115m</sup> In	3.33 · 10 <sup>-15</sup>	1.61 · 10 <sup>-4</sup>	6.78 · 10 <sup>-4</sup>	2.57 · 10 <sup>-6</sup>
<sup>123</sup> I	2.77 · 10 <sup>-16</sup>	2.05 · 10 <sup>-3</sup>	2.81 · 10 <sup>-3</sup>	4.95 · 10 <sup>-7</sup>
<sup>124</sup> I	2.34 · 10 <sup>-16</sup>	1.93 · 10 <sup>-2</sup>	3.21 · 10 <sup>-3</sup>	3.95 · 10 <sup>-6</sup>
<sup>125</sup> I	2.02 · 10 <sup>-18</sup>	4.58 · 10 <sup>+1</sup>	4.39 · 10 <sup>-3</sup>	3.10 · 10 <sup>-7</sup>
<sup>167</sup> Tm	2.79 · 10 <sup>-17</sup>	2.01 · 10 <sup>+2</sup>	3.18 · 10 <sup>-3</sup>	2.81 · 10 <sup>-6</sup>
<sup>193m</sup> Pt	3.40 · 10 <sup>-17</sup>	8.19 · 10 <sup>-2</sup>	1.04 · 10 <sup>-3</sup>	3.20 · 10 <sup>-6</sup>
<sup>195m</sup> Pt	7.15 · 10 <sup>-17</sup>	1.39 · 10 <sup>-3</sup>	8.08 · 10 <sup>-4</sup>	4.37 · 10 <sup>-6</sup>
<sup>212</sup> Bi	2.91 · 10 <sup>-13</sup>	8.21 · 10 <sup>-4</sup>	2.56 · 10 <sup>-3</sup>	3.10 · 10 <sup>-5</sup>
<sup>211</sup> At	2.52 · 10 <sup>-14</sup>	6.53 · 10 <sup>-3</sup>	5.37 · 10 <sup>-3</sup>	4.06 · 10 <sup>-5</sup>
<sup>255</sup> Fm	9.44 · 10 <sup>-15</sup>	4.23 · 10 <sup>-3</sup>	2.91 · 10 <sup>-3</sup>	2.16 · 10 <sup>-5</sup>
Without Auger and Coster-Kronig electrons				
<sup>212</sup> Bi	3.56 · 10 <sup>-13</sup>	1.15 · 10 <sup>-3</sup>	2.76 · 10 <sup>-2</sup>	5.55 · 10 <sup>-4</sup>
<sup>211</sup> At	2.52 · 10 <sup>-14</sup>	8.92 · 10 <sup>+1</sup>	1.00 · 10 <sup>-1</sup>	2.42 · 10 <sup>-3</sup>
<sup>255</sup> Fm	9.41 · 10 <sup>-15</sup>	2.28 · 10 <sup>-2</sup>	2.84 · 10 <sup>-2</sup>	6.71 · 10 <sup>-4</sup>

## REFERENCES

- Snyder WS. Absorbed dose per unit cumulated activity for selected radionuclides and organs. NM/MIRD Pamphlet No. 11, New York: Society of Nuclear Medicine, 1975.
- Loevinger R, Budinger TF, Watson EE, in collaboration with MIRD committee. MIRD primer for absorbed dose calculations. New York: Society of Nuclear Medicine, 1980.
- Task Group Committee 2 of the International Commission on Radiological Protection: Radiation Dose to Patients from Radiopharmaceuticals, ICRP Publication No. 53, Oxford, Pergamon Press, 1988.
- Atkins HL. Potential future application with therapeutic agents. Semin Nucl Med 1979; 9: 121.
- Adelstein SJ, Kassis AI. Radiobiological implications of the microscopic distribution of energy from radionuclides. Nucl Med Biol 1987; 14: 165.
- Howell RW. The MIRD scheme: From organ to cellular dimension. J Nucl Med 1993; 35: 531.
- Rao DV, Nara VR, Howell RW, Govelitz GF, Sastry KS. In-vivo radiotoxicity of DNA-incorporated I-125 compared with that of densely ionizing alpha-particles. Lancet 1989; 2: 650-3.
- Martin RF, Haseltine WA. Range of radiochemical damage to DNA with decay of iodine-125. Science 1981; 213: 896.
- Martin RF, Holmes N. Use of an <sup>125</sup>I-labelled DNA ligand to probe DNA structure. Nature 1983; 302: 452.
- Martin RF, Murray V, D'Cunha G, et al. Radiation sensitization by an iodine-labelled DNA ligand. Int J Radiat Biol 1990; 57: 939.
- Humm JL, Cobb LM. Nonuniformity of tumor dose in radioimmunotherapy. J Nucl Med 1990; 31: 75.
- Bardiès M, Myers MJ. A simplified approach to alpha dosimetry for small spheres labelled on the surface. Phys Med Biol 1990; 35: 1551.
- Humm JL, Chin LM. A model of cell inactivation by alpha-particle internal emitters. Radiat Res 1993; 134: 143.
- Howell RW. Radiation spectra for Auger-electron emitting radionuclides; Report No. 2 of AAPM Nuclear Medicine Task Group No. 6. Med Phys 1992; 19: 1371.
- Howell RW, Rao DV, Hou DY, Narra VR, Sastry KS. The question of relative biological effectiveness and quality factor for Auger emitters incorporated into proliferating mammalian cells. Radiat Res 1991; 128: 128.
- Mausner LF, Srivastava SC. Selection of radionuclides for radioimmunotherapy. Med Phys 1993; 20: 503.
- Smith PHS, Taylor DM. Distribution and retention of the antitumor agent <sup>195m</sup>Pt-cis-dichlorodiammine platinum (II) in man. J Nucl Med 1974; 15: 349.
- Thatcher N, Sharma H, Harrison R, et al. Blood clearance of three radioactively labelled platinum complexes: cis-dichlorodiammine platinum II, cis,trans-dichlorodihydroxy-bis-(isopropylamine)platinum IV and cis-dichloro-bis-cyclopropylamine platinum II in patients with malignant disease. Cancer Chemother Pharmacol 1982; 9: 13.
- Los G, Mutsaers PHA, Lengler WJM, et al. Platinum distribution in intraperitoneal tumors after intraperitoneal cisplatin treatment. Cancer Chemother Pharmacol 1990; 25: 389.
- Deepak A, Wolf W. A new semi-automated system for micro-scale synthesis of [<sup>195m</sup>Pt]cis-platin suitable for clinical studies. Appl Rad Isotopes 1992; 43: 809.

21. Bigler RE, Zanzonico PB. Adjuvant radioimmunotherapy for micrometastases. Srivastava SC, ed. Radiolabeled monoclonal antibodies for imaging and therapy, In: Plenum, New York; 1988: 409.
22. McLaughlin WH, Thramann Jr WM, Lambrecht RM, Milius RA, Bloomer WD. Preliminary observations of malignant melanoma therapy using radiolabeled alpha-methyltyrosine. *J Surg Oncol* 1988; 37: 192.
23. Link EM, Carpenter RN.  $^{211}\text{At}$ -methylene blue for targeted radiotherapy of human melanoma xenografts: Treatment of cutaneous tumors and lymph node metastases. *Cancer Res* 1992; 52: 4385.
24. Stepanek J. A method to determine the radiation spectra due to a single atomic-subshell ionization by a particle or due to decay of radionuclides. Proceedings of SGSMP/SGBT-annual meeting, Villigen, Switzerland, 1993.
25. Stepanek J. A program to determine the radiation spectra due to a single atomic-subshell ionisation by a particle or due to de-excitation or decay of radionuclides. *Comp Phys Comm* (accepted for publication).
26. Tuli JK. Evaluated nuclear structure data file. Brookhaven National Laboratory report BNL-NCS-51655-Rev. 87, 1987.
27. Cullen DE, Perkins ST. The 1991 Livermore evaluated atomic data library (EADL). Lawrence Livermore National Laboratory, Livermore, CA, (to be published).
28. Terrissol M, Pomplun E. Computer simulation of DNA-incorporated  $^{125}\text{I}$  Auger cascades and of the associated radiation chemistry in aqueous solution. *Radiat Prot Dosim* 1994; 52: 177.
29. Knespl D, Reist HW, Stepanek J. Particle track simulation in nanometer range for radiotherapy and radiation protection. Proceedings of SGSMP/SGBT-Annual meeting, Villigen, Switzerland, 1993.
30. GEANT Team, GEANT Version 315, Cern-Data Handling Division, DD/EE/84-1, Revision, 1992.
31. Cullen DE, Perkins ST, Rathkopf JA. The 1989 Livermore evaluated photon data library (EPDL). Lawrence Livermore National Laboratory, Livermore, CA, Report UCRL-ID-103424, 1990.
32. Perkins ST, Cullen DE, Seltzer SM. Tables and graphs of electron-interaction cross sections from 10 eV to 100 GeV derived from LLNL evaluated nuclear data library (ENDL),  $Z = 1 - 100$ . Lawrence Livermore National Laboratory, Livermore, CA, Report UCRL-50400, Vol. 31, 1991.