LOMONOSOV MOSCOW STATE UNIVERSITY
SKOBELITSYN INSTITUTE OF NUCLEAR PHYSICS

A.V.Tultaev, O.V.Fotina, O.A.Yuminov, P.V.Gorbunov, D.O.Eremenko, S.Yu.Platonov

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Abstract

In this work we discuss the methods of radiation dose estimations of the patient with use of given biological tests data.

А.В. Тултаев*,О.В. Фотина, О.А. Юминов, П.В. Горбунов, Д.О.Еременко
С.Ю.Платонов

Оценка поглощенных доз в полых органах человека при использовании α - эмиттерных радиофармпрепаратов

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Аннотация

Настоящая работа посвящена способам оценки поглощенных доз для, так называемого, “эталонного” человека по данным биологических испытаний на животных.

Abstract

The methods of absorbed dose estimation in human organs from incorporated α-emitter radiopharmaceuticals are discussed. We investigate the gender dependence for absorbed doses in a human thyroid gland and for the equivalent effective doses. The methods of absorbed dose estimations in hollow organs of a patient with use of the biological test data are discussed. The estimations are based on the "standard" human phantom.

1 Introduction

One of promising directions in nuclear medicine is α-emitting radiopharmaceuticals (RP) which have some appreciable advantages compared to γ-and $\beta^{\pm}$-emitters [1]. α-particles have a high linear energy transfer in biological tissue and high relative biological efficiency that allows one to increase a radiation dose in tumor per unit of activity incorporated into a patient. α-emitting RP is apparently the best for targeted radiotherapy because of the small α-particles range. With the successful choice of the carrier they can completely lose their energy in a tumor, without a damaging of living tissue.

At the present time ^{211}At is one of the most promising α-emitting isotopes for clinical use. Its properties (including its behavior in living organisms) are given in work [1]. On the other hand, the thyroid carcinoma radioiodine therapy has a wide clinical use and plays an essential role after surgical treatment. For half century history of radioactive iodine application (as an example, ^{131}I) the different methods were worked out for thyroid carcinoma diagnostics and treatment. They are based on histogenetic nature, histological structure and functional influence of the cancer. However, using the ^{131}I-labled RP leads to rather high irradiation upon a patient because of a long half-life time of this isotope and of the hard penetrating its β- and γ- radiations. Besides, the large lengths of absorption of the β- and γ- radiations do not allow one to provide the locality of influence on tumor tissue. There is an essential internal irradiation of healthy organs while an isotope ^{131}I is administrated. Thus, one of the radioiodine therapy disadvantages (limiting its application) is rather high doses for whole body and red marrow. Astatine is chemically analogues of iodine and there is basis to assume that Astatine-labeled pharmaceuticals can be more effective in thyroid gland carcinoma therapy.

In worldwide clinical practice the application of RP is actively developed not only in

diagnostic, but also in the therapeutic purposes. Now, many laboratories in the whole world develop a new line of α-emitting RP. This entails heightened requirements to the radiation dose estimations for separate organs and also for the body as whole. We investigate the RP "Astatine-211" (^{211}At in isotonic solution) for treatment of iodine-dependent types of thyroid carcinoma.

To estimate the clinical therapeutic importance of radiopharmaceuticals, used for targeted radiation therapy, it is important to define a correlation of the RP absorbed doses in pathological organ with one in other, healthy organs and tissues. In particular, for a thyroid gland treatment with α-emitters, it is necessary both to plan and to assess absorbed dose for the thyroid gland and other patient organs. As an initial data we use the data of biological test with rats. In such biological tests the activities in separate organs were measured.

In this work we discuss the methods of absorbed dose (AD) estimations in hollow organs of the patient with use of the biological test data. Also we investigate a probable gender – dose correlation. For these purposes, firstly, we use the results of biological tests of “Astatine-211” RP [2,3], carried out in State Research Center of Russia «Institute of Biophysics» and in the N.N.Blohin Russian Oncology Centre. (The aim of these experiments was to develop the radiopharmaceutical ^{211}At in isotonic solution for treatment of thyroid gland carcinoma.) Secondly, we estimate internal dose by means of the accepted «standard phantoms» of an adult man and a 5-years-old child. Within the phantom the body of the standard human conditionally consists of 26 organs [4,5].

2. Investigation of animal gender influence on the dose prediction.

Fig. 1 shows the ^{211}At accumulation in a thyroid gland and in a wall of a stomach, obtained for both genders as function of the time after administration of RP in a tail vein of a rat. It is clearly seen, “Astatine-211” RP accumulation in thyroid gland depends on gender. This difference cannot be neglected even in view of the experimental uncertainties (Fig. 1a). The influence of gender for stomach (see Fig. 1b) can be neglected.

In the Table 1 we present integrated activity for 10 rat organs with well-defined pharmacokinetic data [2,3]. Here we present the averaged by gender integrated activity data. In addition, the activity for thyroid gland as for males and females are shown.

Let's consider whether these distinctions in integrated activity influence on internal dose estimation in human organs. For this purpose we performed calculations of internal dose for adult standard man with three variants of pharmacokinetics of the pharmaceutical: for males, females and the average one. The results of the calculations are given in Figure 2.

Our result implies that gender effects the equivalent dose (ED) value only for six organs - red

marrow, thyroid gland, bone surfaces, skin, muscular tissue and thymus gland. The ED calculations are performed with the factors considering the relative biological efficiency of α-radiation.

The gender influences also the effective equivalent dose (EED) which is equal to 140 mSv for males, 310 mSv for females and 230 mSv in the average case. The EED values are determined by MIRD method and calculated for 1 MBq of injected activity. The values of the weight factors (which characterize organ sensitivity to stochastic effects of radiation) were taken from [6]. The uncertainties of obtained EED do not exceed 40%.

Thus it is important to take into account a gender in estimation of thyroid gland AD and also in estimation of EED as whole. It should be also noted, that the gender influence is important in measurements of thyroid gland pharmacokinetics of RP in the biological tests with animals.

3. The absorbed dose estimations for hollow organs.

Hollow organs are the organs with separate wall and content regions (in our case, intestines, urinary bladder, heart, gold bladder and stomach). The formula for calculation of AD (see, for example, [2]) for hollow organs is:

$$D_{h.o} = \frac{kA\sum_i n_i E_i \Phi_i^{ts}}{M}$$

where:

$D_{h.o.}$ = absorbed dose in a target organ (rad or Gy)

i = index designating of radiation α, $\beta^{\pm}$, γ;

A = cumulated activity (CA) (sum of all nuclear transitions that occurred) in a source organ (μCi-hr or MBq-s).

n = number of radiations with energy E emitted per nuclear transition;

E = the energy per radiation (MeV);

Φ^{ts} = absorbed fraction (fraction of radiation energy from source organ (s) which absorbed in target (t));

M = mass of target region (g or kg);

k = proportionality constant (rad-g/μCi-hr-MeV or Gy-kg/MBq-sec-MeV)

We consider three possible ways of the absorbed dose estimation for hollow target organs corresponding the methods of the activity registration in hollow organs:

(a) The cumulated activity is registered directly in a wall of the hollow organ. The data are taken from the biological tests of RP with animals. In this case for all types of nonpenetrating (α, β±) radiation: $\Phi_i^{ts}=1$, $M=m_w$, where m_w is weight of wall of the hollow organ.

(b) The cumulated activity is measured simultaneously both in a wall and in contents (measurements of the patient, for example, by a shielding method). For this case Φ_α^{ts} =1.005,

$\Phi_{\beta\pm}^{ts}$=1.5, M=m_w+ m_{cont}, where m_{cont} is weight of hollow organ content.

(c) The cumulated activity is in content of hollow organ (as in the standard method realized in MIRDOSE 3.1 [4,5]). Φ_{α}^{ts} = 0.005, $\Phi_{\beta\pm}^{ts}$ =0.5 and M=m_{cont}.

For modeling of the influence of the various sizes and various weights of organs we use the standard phantoms of five-year child and adult man. The data on activity are taken also from work [2,3].

In Fig. 3 we present the results of AD calculations for five hollow organs with three variants of activity distribution (see above). In the Fig. 3a the estimations for the phantom of five-year child are shown, in the Fig. 3b – the same for adult man.

The EED estimations (per unit of administrated activity) for above two phantoms are given in the table 2.

This analysis shows:

1. The absorbed dose values estimated for all hollow organs by the methods (a) and (b) exceed the absorbed dose obtained by the method (c). The difference reaches 3 orders of magnitude (fig. 3 a,b).

2. The difference in the EED estimations is not so essential, but nevertheless it is up to 30 % (tab. 2).

3. The effect of different estimation method weakly depends on organ size and mass.

The results indicate that: in the estimation of radiation doses in hollow organs, it is necessary to take into account that activity either accumulates in the organ walls or uniformly distributes between walls and contents. Apparently, the absorbed dose calculations standard of nonpenetrating radiation for hollow organs should be reconsider.

3 Conclusions

- During the “Astatine-211” applications the animal gender plays an essential role in estimation of both the thyroid radiation dose and EED. It means that it is necessary to take into account the gender influence in biological tests for any RP developed for the thyroid gland treatment.
- In the estimation of radiation doses in hollow organs for α-emitting RP, one should take into account that total amount of activity is either accumulated in organ walls (as in dosimetry of organs during biological tests) or distributes uniformly between walls and contents (as in dosimetry of real patient).
- Apparently, it is necessary to reformulate the standard method used in the calculation of the absorbed doses in hollow organs in the case of RP with an essential fraction of nonpenetrating

radiation (α, $\beta^{\pm}$). Not so long time ago RP were used mainly for diagnostic purposes. The significant fraction of its radiation is gamma-quanta. In this case, the assumption that the overwhelming fraction of activity accumulates in the hollow organ content does not lead to significant error. The present analysis shows that the situation changes radically in the case of using RP with essential fraction of α radiation.

Acknowledgements

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Table 1. Values of cumulated activity in rat organs (MBq·s)

Table 2. Effective equivalent dose per 1 MBq of injected activity for three estimation methods.

Figure 1. Pharmacokinetics of RP “Astatine-211” for a thyroid gland (a) and for stomach (b): 1 - average values for females, 2 - average values for males

Figure 2. The equivalent dose estimation in human organs with use of pharmacokinetics: *(m)* - for males, *(av)* – average value, *(f)* - for females (1 – red marrow, 2 - thyroid, 3 - breasts, 4 – bones, 5 – skin, 6 – muscle, 7 – thymus).

Figure 3. The hollow organs absorbed dose for different estimation methods (see in the text): a) – phantom of adult man; b) – phantom of five-year-old child. (1 - stomach, 2 - urinary bladder, 3 - small intestine, 4 – upper large intestine , 5 - low large intestine).

Organs	CA (MBq·s)
Stomach	5620
Kidneys	390
Liver	2300
Lungs	890
Spleen	470
Thyroid gland: Males	3900
Females	8800
Average	6500
Body (Remainder)	2500
Heart	107
Brain	51
Urine Bladder	219

Table 1.

Estimation methods	EED (5-year child), mSv	EED (adult man), mSv
(a)	580	390
(b)	500	300
(c)	460	260

Table 2.

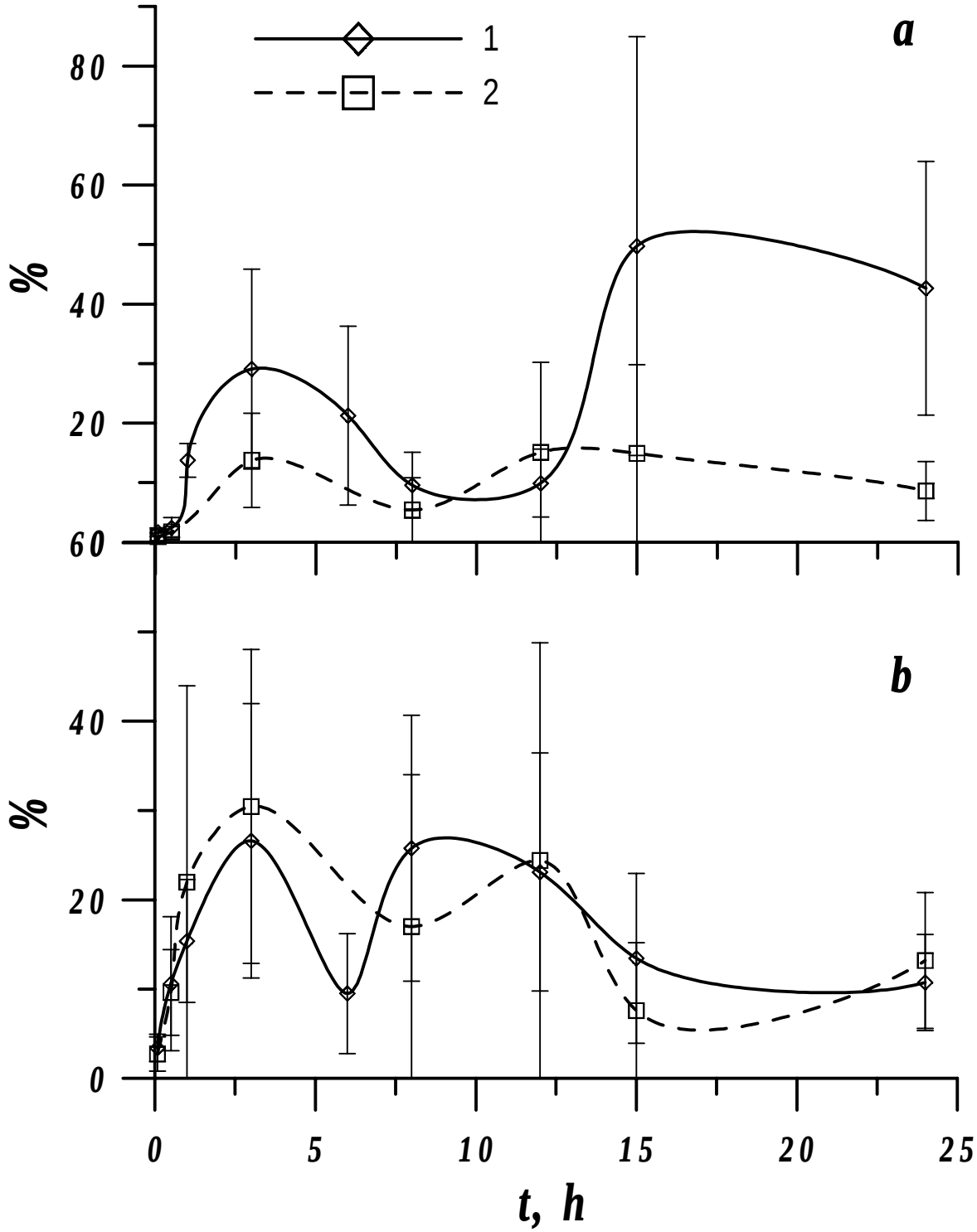

Fig. 1.

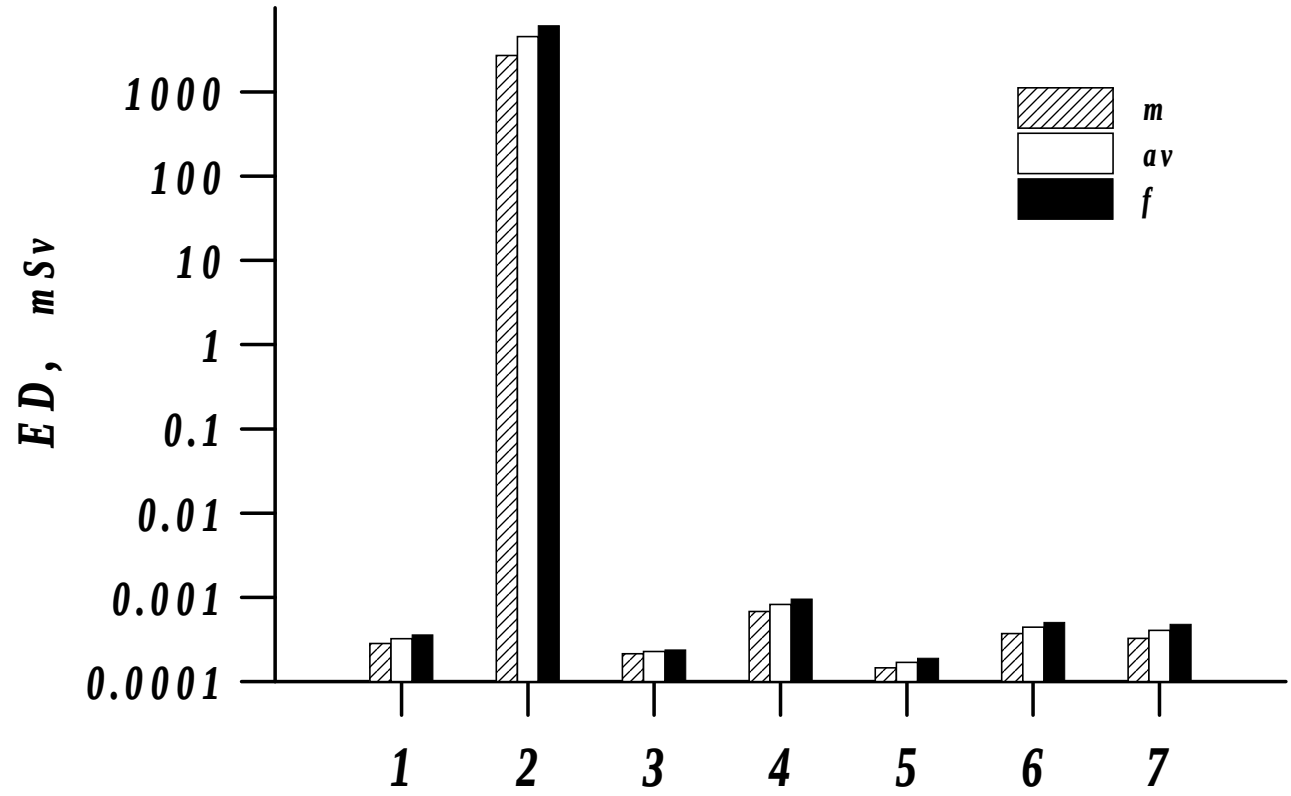

Fig. 2.

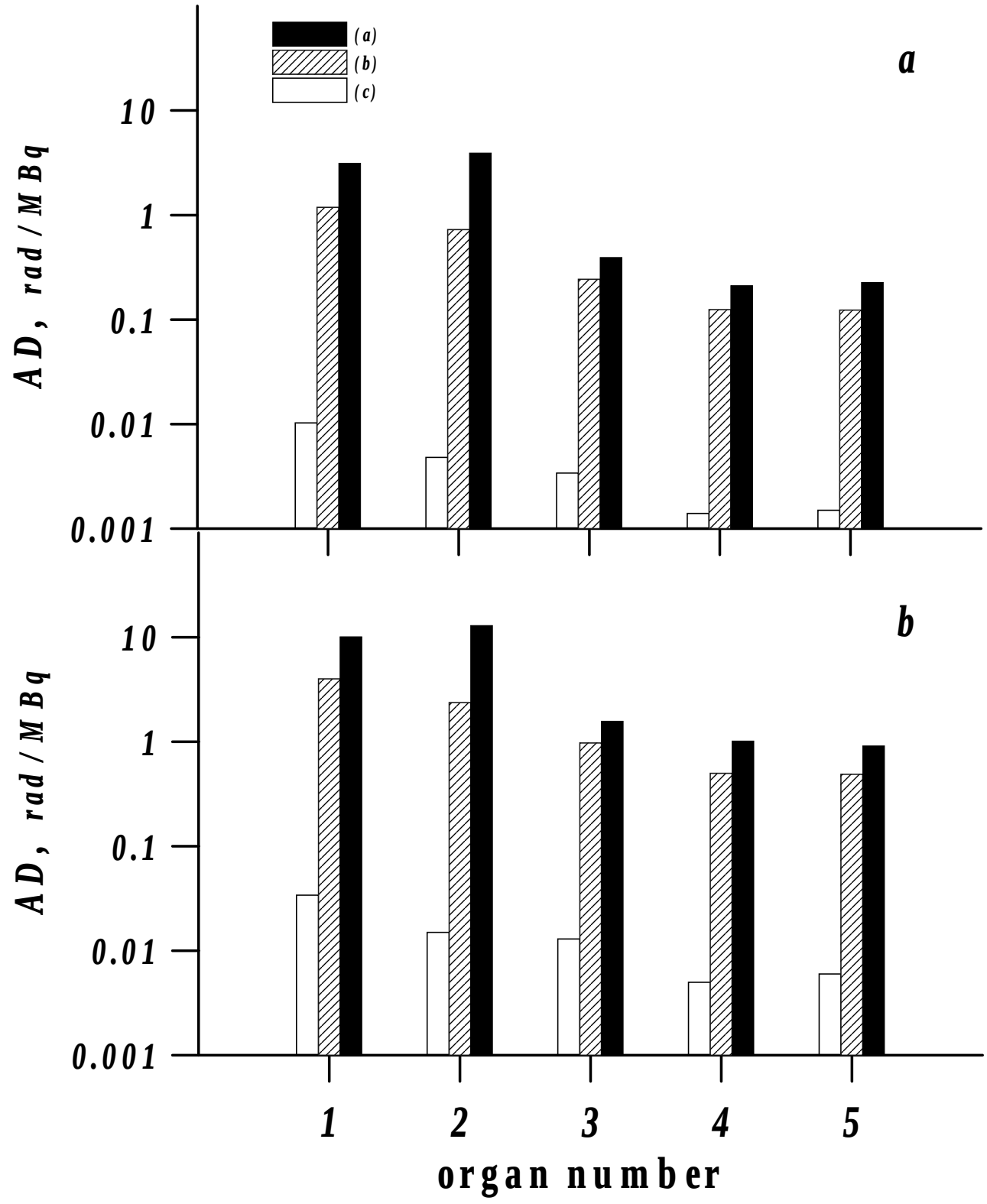

Fig.3

Фотина Ольга Владиленовна
Горбунов Петр Владимирович
Еременко Дмитрий Олегович
Платонов Сергей Юрьевич
Юминов Олег Аркадиевич
Тултаев Антон Васильевич

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