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QUANTITATIVE EVALUATION OF THE PURIFYING ORGANS FUNCTION IN NUCLEAR MEDICINE: THE MEMORY OF THE FUTURE

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The disciplines of medicine and physics are like oil and vinegar, often shaken together, often appetizing but not easily miscible. We attempt to blend the soothing oil of medicine with the acid reality of physics in a study of how the kidney works.
Lloyd Luke, 1971

Abstract. *This paper is the presentation of the fundamentally new approach to the quantitative assessment purifying functions of an excretory organ based on the modern dynamic radionuclide studies. The indicator of the function state of the organ is the relative fraction of the minute circulation volume, which completely cleared by the tested organ – the effective fraction of cardiac output (EFMO), calculated from the activity-time curve, recorded over the heart after injection into the blood circulation of the testing radiopharmaceutical.*
Keywords*: nuclear medicine, dynamic radionuclide studies, purifying organs, cleaning function test*

In the recent decades, clinical radiology received unprecedented technological progress gifted by physicists. Physicists have created and perfected CT, HRCT, PET, SPECT, MRI, functional MRI, digital ultrasound, PET-CT. These new diagnostic modalities gave to physicians the ability to see not only the finer details of the anatomical structure of the internal organs and tissues of the patient, but also the mechanical properties of tissue and the mechanics of the processes of the blood circulation compared norm and pathology [1-9].

However, nuclear medicine studies of the dynamic functional processes, of the principles and the models which have been developed by physicists together with the clinicians at 60-90th years of the last century [10-18], unfortunately, remained on the roadside of the progress. This section of Clinical Radiology, whose development requires cooperation of medical researchers and physicists is used in clinical practice at a level that is too far from his significance in the clinical management of patients [19]. In addition, the cost of new technologies remained aside, and, that is the

principal impossibility, the latest technology are untenable to record of dynamic processes in the body during sufficient time (an hour or even more) that correctly to determine quantitatively of the dysfunction level.

The greatest success in nuclear medicine link of the clinical radiology have been made to create mathematical models and their practical testing for quantitative assessment of the common blood circulation and excretory organs, including the kidneys and the liver [20-28].

This paper presents the further improvement of the principles of quantification of the excretory organs function indices using the dynamic nuclear medicine tests. The impetus for this is the emergence of new radiopharmaceuticals, specifically eliminated from the blood by the different ways.

Let us consider the case of radionuclide study where using the radiopharmaceutical (RPh) that specifically removed from the blood by the examined organ (hereinafter − purifying organ). A curve of the RPh concentration in the blood in time (activity-time curve) recorded above an organ through which the vessels the circulating blood transits, e.g. the heart (hereinafter − the transit organ).

It is obvious that at the first pass through the transit organ RPh activity, present in the moment t in this organ, is the difference between the activity of the RPh, entered at this point of time in the transit organ ($a_i(t)$) and the activity of the RPh extruded from it ($a_o(t)$).

Therefore, activity-time curve R(t) can be written in such equation:

$$R(t) = k(a_i(t) - a_o(t)), \qquad (1)$$

where **k** − the proportionality factor between the RPh activity present in the organ, and the count rate recorded above organ of this time.

Obviously, the value of $\mathbf{a_i(t)}$ is equal to the product of two quantities – total activity of the injected RPh and the likelihood that the transit times of the RPh molecules to entry into the transit organ is less than or equal to **t**. This probability is a function of the distribution of transit times RPh molecules from its point of the injection to the entrance of the transit organ, i.e.:

$$a_i(t) = AF_i(t),$$

where $\mathbf{F_i(t)}$ − the above distribution function, A − total activity of the injected RPh.

Similarly:

$$a_o(t) = AF_o(t),$$

where $F_o(t)$ − distribution function of the transit times of the RPh molecules from its point of the injection to the exit from the transit organ.

Then we can write from (1):

$$R(t) = kA(F_i(t) - F_o(t)).$$

So let us calculate the area under the curve of the first pass RPh through the transit organ:

$$S_0 = \int_0^\infty R(t)dt = kA\int_0^\infty (F_i(t) - F_o(t))dt \qquad (2)$$

and convert the equation:

$$\int_0^\infty (F_i(t) - F_o(t))dt = t(F_i(t) - F_o(t))\Big|_0^\infty - \int_0^\infty t(f_i(t) - f_o(t))dt. \qquad (3)$$

Because $F_i(\infty) \equiv 1 \equiv F_o(\infty)$, the first term of the right-hand side of (3) is equal to zero, therefore:

$$\int_0^\infty (F_i(t) - F_o(t))dt = \int_0^\infty tf_o(t)dt - \int_0^\infty tf_i(t)dt = \bar{t}_o - \bar{t}_i, \qquad (4)$$

where $\bar{t}_i$ and $\bar{t}_o$ are average transit times from the point of introduction of the RPh to an entrance of the transit organ and to an exit from it, respectively.

It is obvious that $\mathbf{t_o = t_i + t_t}$, where $\mathbf{t_t}$ – transit time of the RPh in the transit organ. As the random variables $\mathbf{t_i}$ and $\mathbf{t_t}$ are independent random variables, we can write:

$$\bar{t}_o = \bar{t}_i + \bar{t}_t \quad \text{or} \quad \bar{t}_t = \bar{t}_o - \bar{t}_i.$$

Comparing the last formula on the right side of (4) and taking into account the expressions (2) and (3), it is easy to understand that:

$$S_0 = kA\bar{t}_t.$$

So, the area under the curve activity-time of first pass of the RPh through the transit organ for any law of RPh entrance in this organ is the product of the administered RPh activity with its average transit time in the transit organ and a

factor of proportionality between the count rate over that organ and RPh activity therein.

One of the most important hemodynamic parameters of the body is the minute volume of circulation (MVC shorter MV), i.e. the volume of blood, flowing through the cavities of the heart per minute. In adult MV is about 5–7 liters per minute.

Ejected by the left ventricle into the aorta the blood is distributed at the network of arteries, delivering it to the organs and tissues. Some part of the MV passes through each organ including through the purifying organs.

The most important of all purifying organs are the kidneys. In a normal adult human about 25% of the blood, ejected by the heart, passes through the kidneys. Such rich blood supply is provided by the anatomy of the renal arteries extending from the abdominal aorta like a short thick trunk.

They distinguish for the kidneys: **total renal circulation** (TRC) – the amount of blood passing through the entire kidney per minute, and **effective renal circulation** (ERC) – blood flow through functioning renal parenchyma per minute, which accounts about 90% of the TRC. TRC has the ability to autoregulation – to remain constant. ERC in renal disease is reduced in proportion to the extent of damage of the kidney purifying function. This in turn leads to lower values of the ratio of ERC/MV in this condition. Consequently, the ratio between the effective renal circulation and minute volume of circulation – ERC/MV – can be a very valid indicator of the kidneys purifying function in all circumstances, moreover independent of all other terms and conditions. In its physiological fact, this figure is the **effective fraction of minute volume of circulation** (EFMV) for the tested purifying organ.

Assessment of the ERC state is carried out by an indirect method of a clearance – measuring the ability of the cells of the renal parenchyma to the almost complete removal of the blood test substances. For this purpose, use of such compounds as paraaminohippuric acid (PAH), diodrast, creatinine. However, this method has some limitations, it is burdensome for the patient and provides significant errors, so the use of this method clinically impractical.

Let the RPh, which selectively extracted by the kidneys, is introduced into the bloodstream. Within a minute the kidneys cleanse out of the RPh from the fraction of the MV which strictly equal to the absolute value of the quantity of the ERC. Further the purified blood returns to the general circulation and reduces the concentration of the RPh in it proportionally to the ratio of ERC/MV. Thus, the ERC in the general circulation can be formally regarded as a fraction of the MV, completely free of the RPh at the same its concentration in the rest of the MV.

Denote the ratio of ERC/MV by the coefficient **φ** and write in the form of the equation: **φ =** ERC/MV = EFMV.

The coefficient **φ** is the probability that the molecule of RPh walk into a purifying organ on the first pass of blood through the circulatory system. Hence the probability $\mathbf{p_n}$ of that the molecule will be captured at the **n**-th pass is calculated as follows:

$$p_n = \varphi(1-\varphi)^{n-1}$$

Now we calculate the total area ($\mathbf{S_c}$) under of the activity-time curve recorded above the transit organ. Since, as above mentioned, when passing through a purifying organ of the RPh portion, corresponding contribution in the total area is not dependent on input law of this portion and is determined only by its activity and the average transit time of the RPh in the transit organ, it can be written:

$$S_c = k\bar{t}_t\left(a_1 + 2a_2 + 3a_3 + ...\right) = k\bar{t}_t \sum_{n=1}^{\infty} n a_n , \qquad (5)$$

where a_1, a_2, a_3, ... – activity of those portions of the RPh that were captured in the first, second, third, etc. drug passes through the circulatory system, respectively.

Clearly, $a_n = Ap_n = A\varphi(1-\varphi)^{n-1}$, therefore taking into account (5) we can write:

$$S_c = kA\bar{t}_t\varphi\sum_{n=1}^{\infty} n(1-\varphi)^{n-1}$$

Transforming the last expression and using the formula for the sum of a geometric progression, we obtain:

$$\sum_{n=1}^{\infty} n(1-\varphi)^{n-1} = \frac{1}{\varphi^2} \quad \text{and} \quad S_c = \frac{kA\bar{t}_t}{\varphi}.$$

From here: $$\frac{S_0}{S_c} = \varphi,$$

i.e. value of the EFMV is the ratio of the area under the curve of the first pass of the RPh through transit organ allocated from recorded above this organ the activity-time curve, to the area under the total activity-time curve.

It deserves to be noted that the simple calculations lead to the following interesting result: $$\frac{1}{\varphi} = \bar{n},$$

that is the inverse of EFMV, equal to the average number of passes of the RPh molecules through the circulatory system until they are captured by purifying organ.

The above principles for determining the level of kidney function by using dynamic radionuclide studies are applicable also to examine of the purifying functions of the liver using proper purpose radiopharmaceuticals.

The authors indicated no potential conflicts of interest.

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Кількісна оцінка функції очисних органів в ядерній медицині: спогади про майбутнє

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Резюме. Стаття стосується викладу принципово нового підходу до кількісної оцінки очисної функції будь-якого екскреторного органу на основі сучасних динамічних радіонуклідних досліджень. Показником стану цієї функції органу є відносна фракція хвилинного об'єму кровотоку, що повністю очищається органом – ефективна фракція хвилинного об'єму (ЕФМО), яка обчислюється по кривій активність-час, реєстрованої над серцем після введення в кровообіг тестового радіофармпрепарата.

Ключевые слова: ядерная медицина, динамические радионуклидные исследования, депурационные органы, тест очистительной фукции

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Количественная оценка функции очистительных органов в ядерной медицине: воспоминания о будущем

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Резюме. Статья касается изложению принципиально нового подхода к количественной оценке очистительной функции любого экскреторного органа на основе современных динамических радионуклидных исследований. Показателем состояния этой функции органа является относительная фракция минутного объема кровотока, полностью очищаемая органом – эффективная фракция минутного объема (ЭФМО), вычисляемая по кривой активность-время, регистрируемой над сердцем после введения в кровоток тестирующего радиофармпрепарата.

Ключові слова: ядерна медицина, динамічні радіонуклідні дослідження, депураційні органи, тест очисної функції

Received: 25.12.2014 *Accepted: 3.03.2015*