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Междисциплинарный банк данных в онкоэндокринологии: радиойодрефрактерный дифференцированный рак щитовидной железы

П.О. Румянцев¹, А.Г. Байдак²¹ Международный медицинский центр «СОГАЗ-МЕДИЦИНА», Санкт-Петербург, Российская Федерация² ООО «М-Дата», Орёл, Российская Федерация

АННОТАЦИЯ

Высокие достижения в персонализированной доказательной медицине, и онкологии в развитых странах связаны с развитием клинических карцер-регистров пациентов (SEER, NCDB и др.), которые представляют собой мультимодальные и междисциплинарные банки данных. Они являются матрицей данных для развития аналитических и прогностических инструментов в изучении особенностей диагностики, клинического течения болезней, ответа на терапию, оценки влияния прогностических факторов и пр. С точки зрения медицинских цифровых банков данных, избыточность и дублированность данных не так критичны, как неполнота или противоречивость информации при принятии медицинских решений.

Цель статьи — анонс мультимодального банка данных пациентов с радиойодрефрактерным дифференцированным раком щитовидной железы, который, по сути, является современным междисциплинарным цифровым медицинским регистром.

Наряду с демографическими и нозологическими данными, характерными для эпидемиологических регистров, в мультимодальных банках данных учитываются ключевые клинические и параклинические данные: результаты лабораторных, морфологических и инструментальных методов исследования, различные методы визуализации (ультразвуковое исследование; компьютерная и магнитно-резонансная томография; однофотонная эмиссионная компьютерная томография, совмещённая с компьютерной томографией; позитронно-эмиссионная томография, совмещённая с компьютерной томографией). В мультимодальных банках данных представлены результаты молекулярно-генетического профиля опухоли, клиническая польза которого в выборе тактики лечения сегодня не подвергается сомнению. Все эти данные накапливаются в мультимодальных банках данных с отметкой о времени выполнения, результатах пересмотра (второе мнение), учёта стандартизированных качественно-количественных параметров (факторов), потенциально влияющих на клиническое течение, ответ на лечение, развитие осложнений и исход.

Ключевые слова: банк данных; мультимодальный карцер-регистр; рефрактерный; дифференцированный; рак щитовидной железы; радиойодтерапия.

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Interdisciplinary databank in oncoendocrinology: radioiodine refractory differentiated thyroid cancer

Pavel O. Rumiantsev¹, Andrey G. Baidak²

¹ International Medical Center "SOGAZ-MEDICINE", Saint Petersburg, Russian Federation

² M-Data, Orel, Russian Federation

ABSTRACT

High achievements in personalized evidence-based medicine and oncology, particularly in developed countries, are associated with the successful development of "clinical" carceral registries of patients (SEER, NCDB, etc.), which are multimodal data banks. They are a data matrix for the development of analytical and prognostic tools in the study of diagnostic features, clinical disease course, therapy response, assessment of prognostic factors, etc. From the point of view of medical digital data banks, data redundancy and duplication are not as critical as information incompleteness or inconsistency when making medical decisions.

This study aimed to present a multimodal database of patients with radioiodine refractory differentiated thyroid cancer, which is essentially a modern interdisciplinary digital medical registry.

Along with demographic and nosological data that is typical for epidemiological registers, the multimodal data banks consider key clinical and paraclinical data, such as the results of laboratory, morphological, and instrumental research methods, and various imaging methods, such as ultrasound, computed tomography (CT), magnetic resonance imaging, single-photon emission computed tomography/CT, and positron emission tomography/CT. The multimodal data banks present the molecular genetic profile results of the tumor, of which the clinical usefulness in the choice of treatment tactics is undoubted today. All these data are accumulated in the multimodal data banks, noting the execution time and the revision results (second opinion), considering standardized qualitative and quantitative parameters (factors) that potentially affect the clinical course, treatment response, complication development, and outcomes.

Keywords: data bank; multimodal; cancer registry; refractory; differentiated; thyroid cancer; radiotherapy.

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肿瘤内分泌学中的多模式数据库： 放射性碘难治性分化型甲状腺癌

Pavel O. Rumiantsev¹, Andrey G. Baidak²

¹ International Medical Center "SOGAZ-MEDICINE", Saint Petersburg, Russian Federation

² M-Data, Orel, Russian Federation

简评

个性化循证医学和肿瘤学方面的高成就，尤其是在发达国家，与成功开发了多模式数据库“临床”癌症患者登记系统（SEER、NCDB 等）有关。它们是用于开发分析和预后工具的数据矩阵，用于研究诊断特征、疾病的临床过程、对治疗的反应、评估预后因素的影响等。从医疗数字数据库的角度来看，在做出医疗决策时，数据的冗余和重复并不像信息的不完整或不一致那么重要。

本文目的是宣布一个放射性碘难治性分化型甲状腺癌患者的多模式数据库，该数据库本质上是一个现代跨学科数字医疗登记系统。

除了流行病学登记的典型人口统计学和疾病学数据外，多模式数据库还考虑了关键的临床和临床旁数据：实验室结果、形态学和仪器研究方法、各种成像方法（超声、CT、MRI、SPECT/CT、PET/计算机断层扫描）。多模式数据库展示了肿瘤分子遗传学谱的结果，其治疗策略选择中的临床实用性在今天是毫无疑问的。所有这些数据都累积在多模式数据库中，并在执行时间、审查结果（第二意见）上进行标记，同时考虑到可能影响临床过程、治疗反应的标准化定性和定量参数（因素），并发症和结果的发展。

关键词：数据库；多模式；恶性肿瘤登记；难治性；分化型；甲状腺癌；放射性碘治疗。

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INTRODUCTION

In Russia, the incidence of thyroid cancer (TC) has increased more than twice the number, from 4.41 per 100,000 populations in 1998 to 9.53 in 2019 [1, 2], primarily due to the additional detection of papillary microcarcinomas resulting from widely used ultrasound (US) examinations.

Approximately, 70%–80% of the presently detected thyroid carcinomas have a favorable prognosis, particularly when detected at early stages. Moreover, postoperative iodine-131 therapy is not indicated for this patient group [3]. On average, 10% of patients with differentiated thyroid cancer (DTC) show radioiodine refractoriness (RR) [4].

INTERDISCIPLINARY DATABANKS

At present, registries for patients with cancer (Surveillance, Epidemiology, and End Results, National Cancer Database, and others) or interdisciplinary databanks (IDB) are the major tools worldwide that are used for studying the features of clinical disease course and therapy response and assessing the influence of prognostic factors [5]. The integration of specialists of different profiles on a single information platform allows rapid communication and expert support for medical decision-making [6]. The primary stakeholder for accurate and rapid medical decision-making is the patient; therefore, patient involvement as a “donor” of anamnestic and operative medical information (extracts, tests, disks, and glasses), both in paper and electronic digital formats, is necessary. Redundancy and data duplication are not critical in terms of medical interactive databanks, whereas incomplete or inconsistent information is critical in medical decision-making.

Therefore, the European Union Committee of Experts on Rare Diseases operates to obtain consolidated data on patients who suffer from rare diseases, including rare cancers with an incidence of <6 per 100,000 population and TC also belongs to it [7]. Currently, Russia has several active registries at different healthcare levels.

INTERDISCIPLINARY PATIENT DATABANK PROJECT FOR RADIOIODINE-REFRACTORY DTC

This study aimed to popularize the Interdisciplinary Patient Databank Project for Radioiodine-Refractory Differentiated TC (IDB RR-DTC), which is essentially a modern clinical registry and is supported by the Association of Endocrine Surgeons (<https://as-endo.ru/>) and the Association for the Development of Theranostics (<https://www.theranostics.pro/>).

Significant clinical and paraclinical data are considered in the developed IDB RR-DTC, namely, results of laboratory,

morphological, and instrumental methods of examination and various imaging techniques (US, computed tomography [CT], magnetic resonance imaging [MRI], single-photon emission CT/CT [SPECT/CT], and positron emission tomography/CT [PET/CT]), in addition to demographic and nosological data characteristic of epidemiological registries. IDB RR-DTC plans to record (when completed) the results of the molecular genetic profile of tumors, which clinical benefit in the choice of treatment tactics is no longer in doubt. All these data will be accumulated in the IDB RR-DTC with a note on the time of execution and revision results (second opinion), including standardized qualitative and quantitative parameters (factors) that potentially influence the clinical course, treatment response, complications, and outcomes.

Several studies showed that tumor growth and TC progression are closely related to somatic point mutations in the *BRAF*, *RAS*, and *RET* genes. These mutations contribute to activating the mitogen-activated protein kinase and phosphoinositide 3-kinase proliferation signaling pathways, which are crucial in TC development [8]. Clinicians should keep in mind that patients with a Bethesda IV, V, and VI cytology report may be prescribed molecular genetic testing in the *BRAF*, *TERT*, *RAS*, *RET/PTC*, and *PAX8/PPAR-γ* genes, as recommended by the Ministry of Health of the Russian Federation [9].

The IDB RR-DTC project collects information on molecular genetic testing results for known mutations in the *BRAF*, *TERT*, *RAS*, *RET/PTC*, and *PAX8/PPAR-γ* genes for subsequent analysis.

The created IDB RR-DTC uses templates for entering anamnestic data (to show data in one form), editing the existing history, adding dated changes, and attaching documents in PDF format.

This databank is an integration project for developing digital medicine to address the following healthcare challenges:

- A multidisciplinary paradigm of multimodal data collection and analysis unified for prompt and evidence-based patient care;
- Digital resource creation that is available to the interested doctor to record and analyze his/her own experience and prompt peer expert support in real clinical practice;
- An innovative digital platform for multicenter scientific and practical research;
- A matrix for clinical and epidemiological research, radiomics development, deep machine learning, and artificial intelligence in medicine;
- New RR-DTC case predictions and their verification and optimal treatment tactic selection;
- Evidence-based experience consolidation in the effective and safe treatment of patients (e.g., surgery, radioiodine therapy, hormone therapy, and targeted therapy).

Table. Structure of data stored and processed in the Interdisciplinary Patient Databank Project for Radioiodine-Refractory Differentiated Thyroid Cancer (IDB RR-DTC)

Section	Parameters
Demographics	Surname, first name, patronymic, date of birth, gender, and address
History	- Family history - Radiation history (neck irradiation and being in a radiation exposure area)
Diagnosis(s)	- ICD-10 code - The histological type of carcinoma
Primary tumor grade	- Tumor grade (TNM and clinical stage) - Parameters of the primary tumor (size, number, invasiveness, histological variant, and characteristics) - Localization, size, and number of metastases (removed/affected), and capsule infiltration
Genetics (tumor)	<i>BRAF</i>, <i>RET</i>, <i>NTRK</i>, <i>TERT</i>, <i>PAX8/PPAR-γ</i>, <i>RAS</i> (mutation detection method, laboratory tests, and results)
Instrumental diagnostics	<i>Date</i> - US - Endoscopy - X-ray <i>Tumor dynamics assessment (RECIST):</i> - CT/MRI (± contrasting) - SPECT/CT) - PET/CT
Surgery	<i>Date of surgery</i> <i>MF</i> - Surgical volume: on the thyroid gland, on regional lymph nodes (including ASL), outside the neck - Use of intraoperative neuromonitoring - Complications (surgical treatment): <i>Date of registration</i> - Postoperative laryngeal paresis/paralysis - Grade of postoperative hypoparathyroidism - Other (specify)
Radioiodine diagnostics (RD) and radioiodine therapy (RT)	<i>Date of procedure</i> <i>MF</i> - Radioisotope: Iodine-123, Iodine-131, and Iodine-124 - Activity (MBq/mKi): automatic recalculation - SPECT/CT) - PET/CT Distribution and accumulation of radiopharmaceuticals in projecting the thyroid bed, regional neck lymph nodes, retroperitoneal lymph nodes, lungs, bones, and other localizations of pathological accumulation The presence of radioiodine-resistant metastases (RR date to be registered), localization and size of foci, and progression (RECIST 1.1.) <i>Complications (RT):</i> - Postoperative laryngeal paresis/paralysis - Grade of postoperative hypoparathyroidism - Other
Laboratory diagnostics	<i>Date of analysis</i> - TTH - FT (4) - TG - TgAb - CEA - Cyfra 21.1 - Proteinuria (AE) - Creatinine (AE) - AspAT (AE) - ALAT (AE)

Table. Ending

Section	Parameters
Laboratory diagnostics	• Bilirubin (AE) • Hemoglobin (AE) • Leukocytes (AE) • Neutrophils (AE) • Platelets (AE)
Histology	<i>Date of examination</i> • # of examination (glass, blocks) • MF • Histological type and carcinoma variant • Size and localization of the dominant tumor in the thyroid • Presence and character of carcinoma intrinsic capsule • Invasion/infiltration of thyroid capsule carcinoma • Carcinoma multifocality in the thyroid • Angioinvasion in the thyroid • Number of removed ASL lymph nodes • Number of metastatic ASL lymph nodes
Hormone therapy	<i>Date of administration</i> • Daily dose, µg
Radioiodine resistance (summary)	RR date (see RD/RT section) Total activity of iodine-131 (including that at which RR was registered, GBq/mKi)
Targeted therapy	<i>Date (administration, correction, and withdrawal)</i> • Drug (INN) • Daily dose, mg • Reasons for drug withdrawal
Adverse events (complications) of targeted therapy	<i>AE registration date</i> • ECOG, st. • Arterial hypertension, st. • Diarrhea, st. • Nausea and vomiting, st. • Fatigue, st. • Decrease in body weight and loss of appetite, st. • Renal toxicity (proteinuria), st. • Rash (hand-foot syndrome), st. • Bleeding threat, st. • Liver toxicity (AspAT, ALAT, bilirubin), st. • Hypothyroidism, st. • Myelosuppression, st.

Note: *TTH*, thyrotropic hormone; *TG*, thyroglobulin; *TgAb*, thyroglobulin antibodies; *FT*, free tetraiodothyroxine; *ASL*, anatomical and surgical level of regional lymph nodes; *MF*, medical facility; *AE*, adverse events.

ACTUAL CONTENT

At present, the IDB RR-DTC project is already available at <http://reestr.medical-data.ru/mbd/> for the general medical community both for review and participation. The accessible version is the result of the efforts of 11 doctors, covering the observation data of 228 patients from 48 regions of the Russian Federation. All doctors who treat patients with RR-DTC, including oncologists, surgeons, radiologists, nuclear medicine specialists, endocrinologists, chemotherapists, pathologists, and geneticists, are welcome to join the project. The developers offer to directly register in the system when entering the website. The IDB RR-DTC interface (Fig. 1) is easy-to-use for any

doctor since the project was designed and implemented by a doctor.

Sections to be filled out correspond to the classic medical history and outpatient records. Doctors can broaden their professional horizons without leaving the workplace, learn teamwork, exchange experience in managing patients with RR-DTC, become involved in scientific and analytical work, and become coauthors of publications in both domestic and foreign scientific medical journals by participating in the project.

The multimodal data bank (clinical, laboratory, and radiological) creation develops and facilitates interdisciplinary collaboration, which, in turn, forms the basis

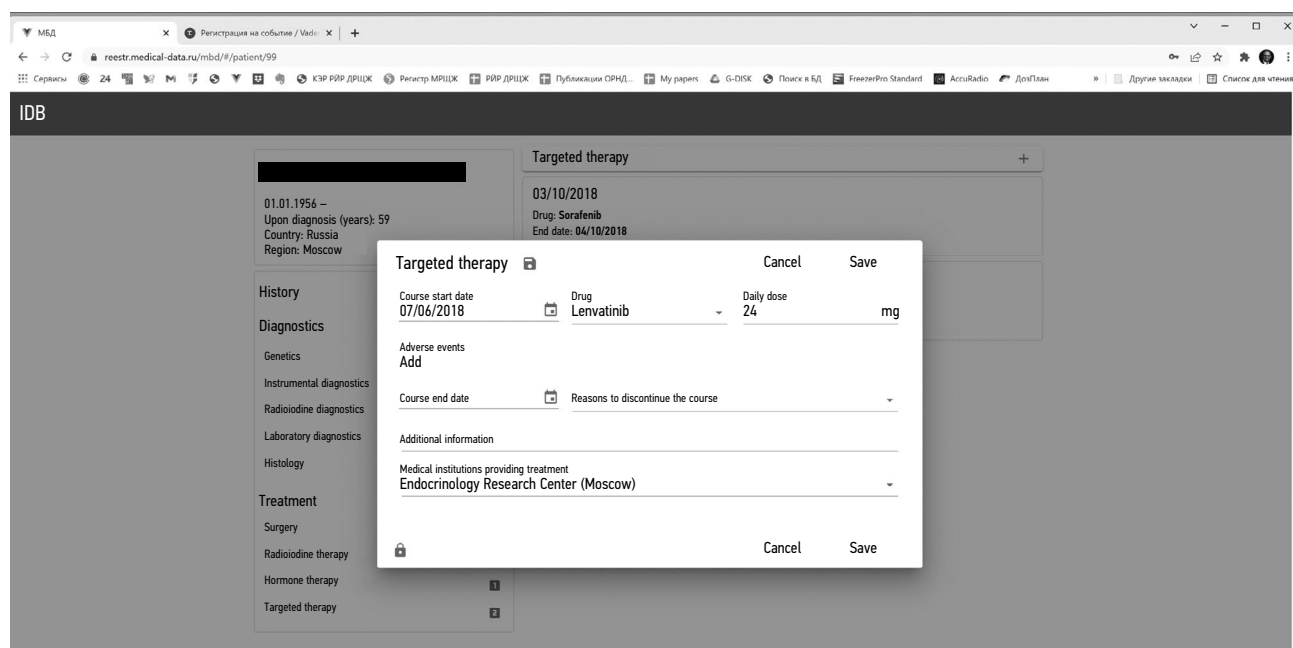


Fig. 1. The interface of the Interdisciplinary Patient Databank Project for Radioiodine-Refractory Differentiated Thyroid Cancer (IDB RR-DTC).

for multicenter and national clinical and epidemiological evidence-based studies and the improvement of diagnostic, treatment, and rehabilitation technologies for patients with cancer. This is true for neuroendocrine tumors that are highly aggressive and refractory to standard disease treatment.

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Authors' contribution. Rumiantsev P.O. — idea, design, content of the article; Baidak A. — figures, technical assistance. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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AUTHORS' INFORMATION

* **Pavel O. Rumiantsev**, MD, Dr.Sci. (Med);
address: 8, Malaya Konyushennaya, Saints Peterburg, Russia,
191186; ORCID: <https://doi.org/0000-0002-7721-634X>;
eLibrary SPIN: 7085-7976; e-mail: pavelrum@gmail.com

Andrey G. Baidak;
e-mail: baidak@medical-data.ru

ОБ АВТОРАХ

* **Румянцев Павел Олегович**, д.м.н.;
адрес: 191186, Санкт-Петербург, Малая Конюшенная, 8;
ORCID: <https://doi.org/0000-0002-7721-634X>;
eLibrary SPIN: 7085-7976; e-mail: pavelrum@gmail.com

Байдак Андрей Геннадьевич;
e-mail: baidak@medical-data.ru

* Corresponding author / Автор, ответственный за переписку