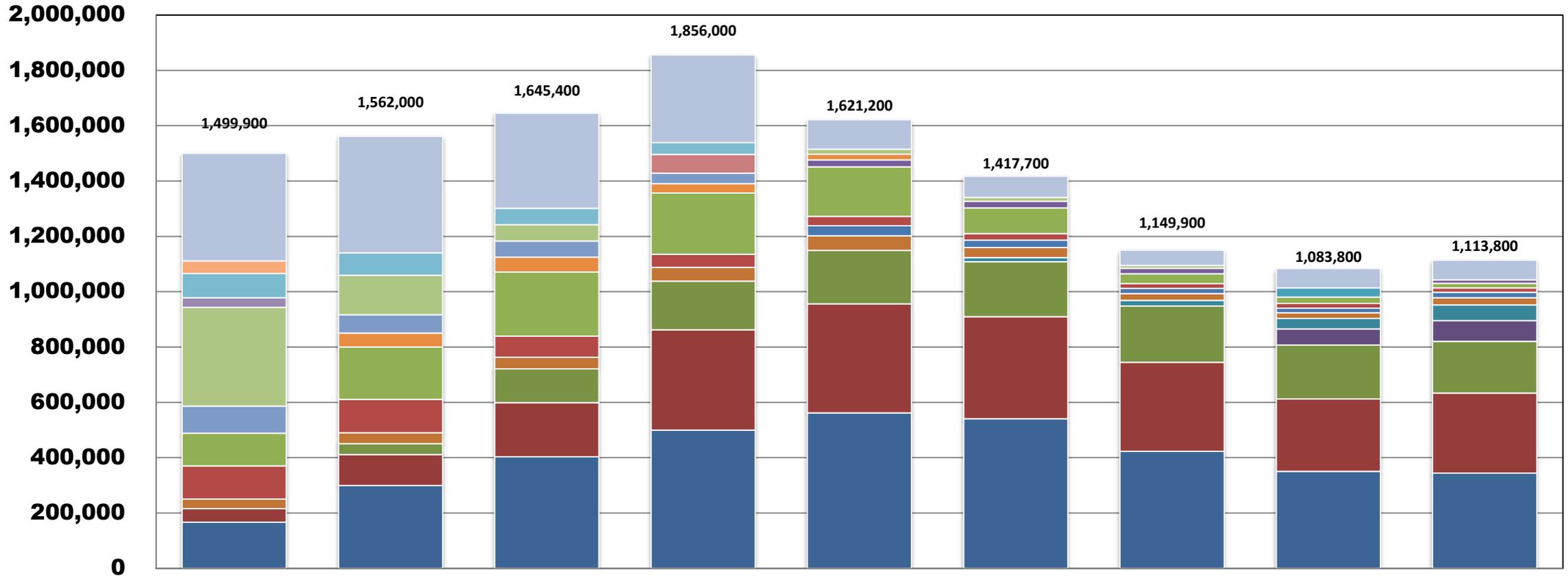


The Action Plan for Promotion of Production and Utilization of Medical Radioisotopes (Outline)

Jun Hatazawa, MD, PhD

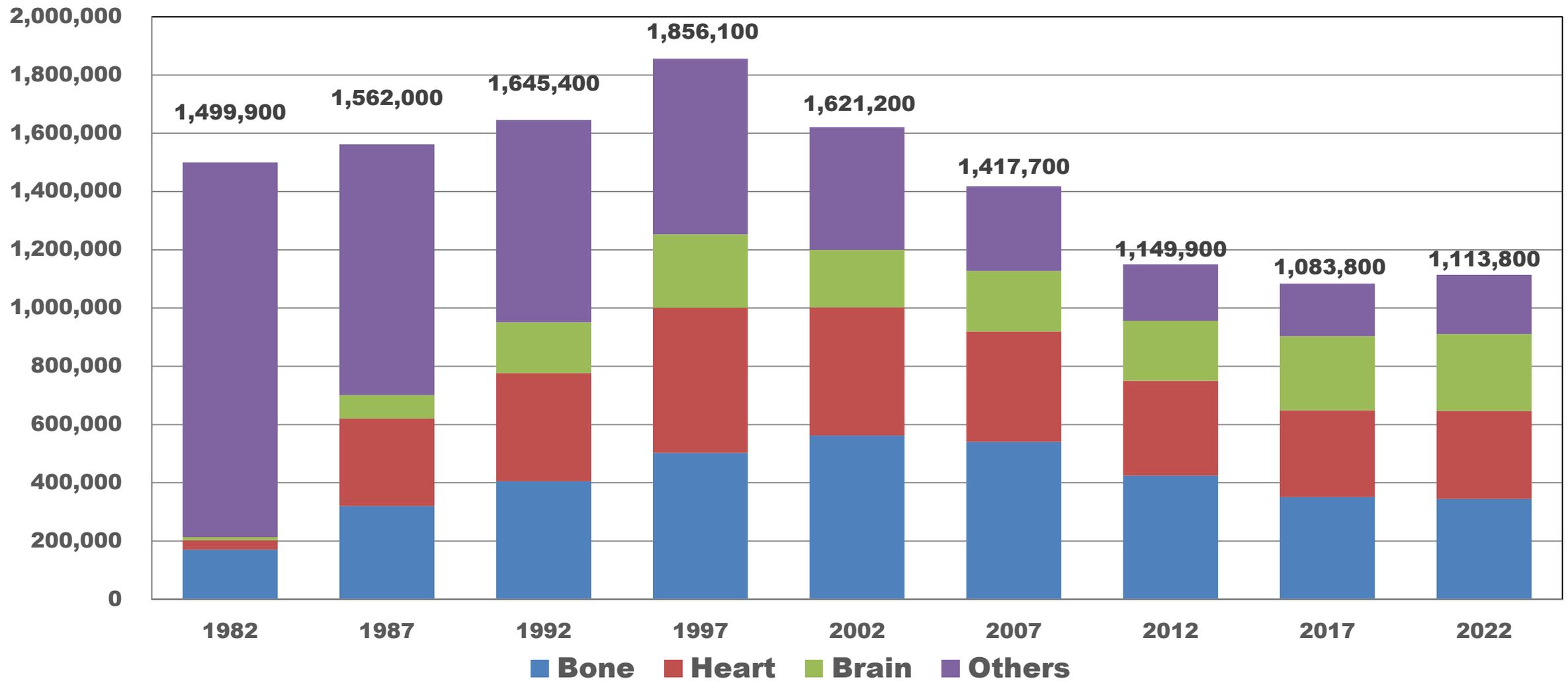
**Special Advisor
Atomic Energy Commission Japan
Chief Executive Director
Japan Radioisotope Association**

Number of single photon emitter tests by categories (Estimated number of examinations in a year)

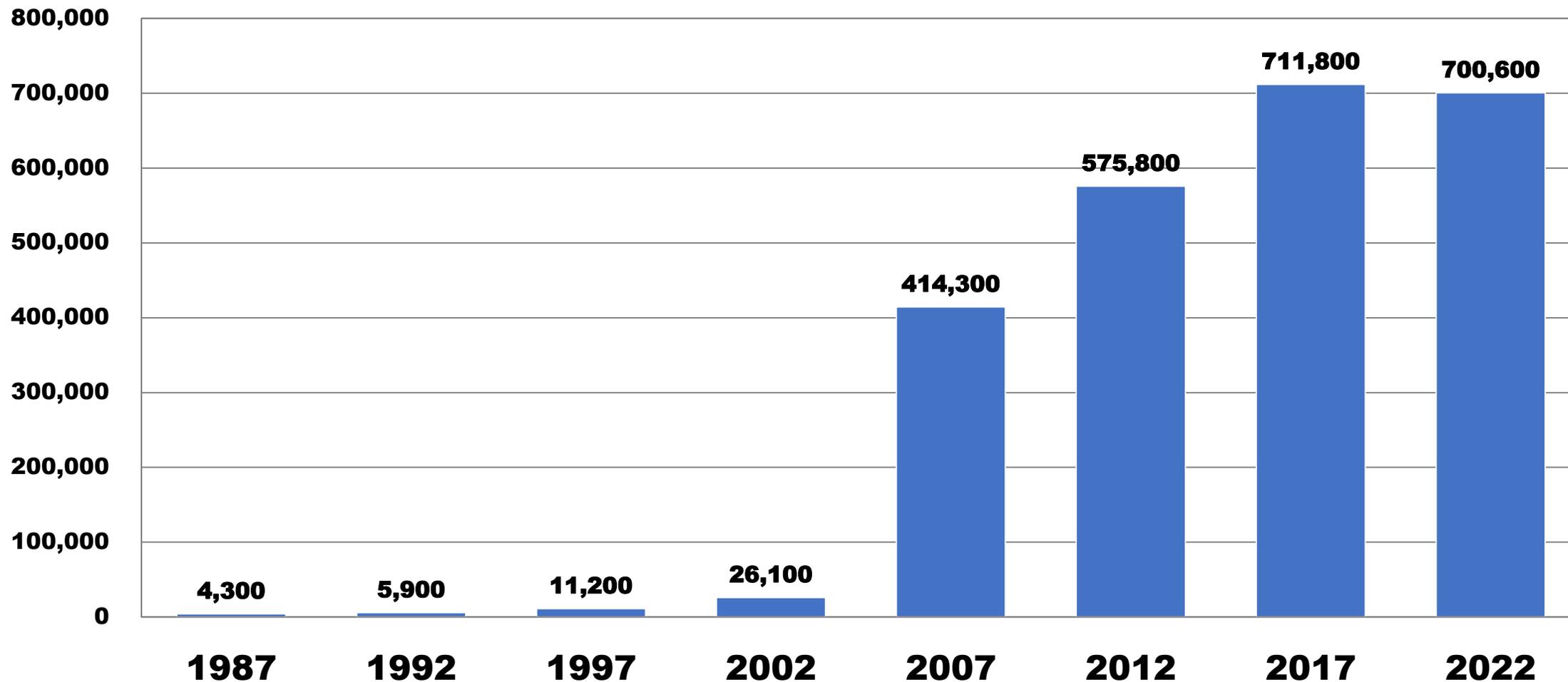


- Bone scintigraphy
- Myocardial perfusion
- Brain perfusion
- Dopamine transporter
- Sentinel lymph node
- Lung perfusion
- Dynamic renal
- Thyroid scintigraphy
- Ga scintigraphy
- Ga inflammation
- MIBG myocardial
- ECG gated pool
- Iodine uptake thyroid
- Xenon CBF
- Liver scintigraphy
- Radionuclide angiography
- Renographm
- Static renal
- Others

Number of single photon emitter tests by categories (Estimated number of examinations in a year)

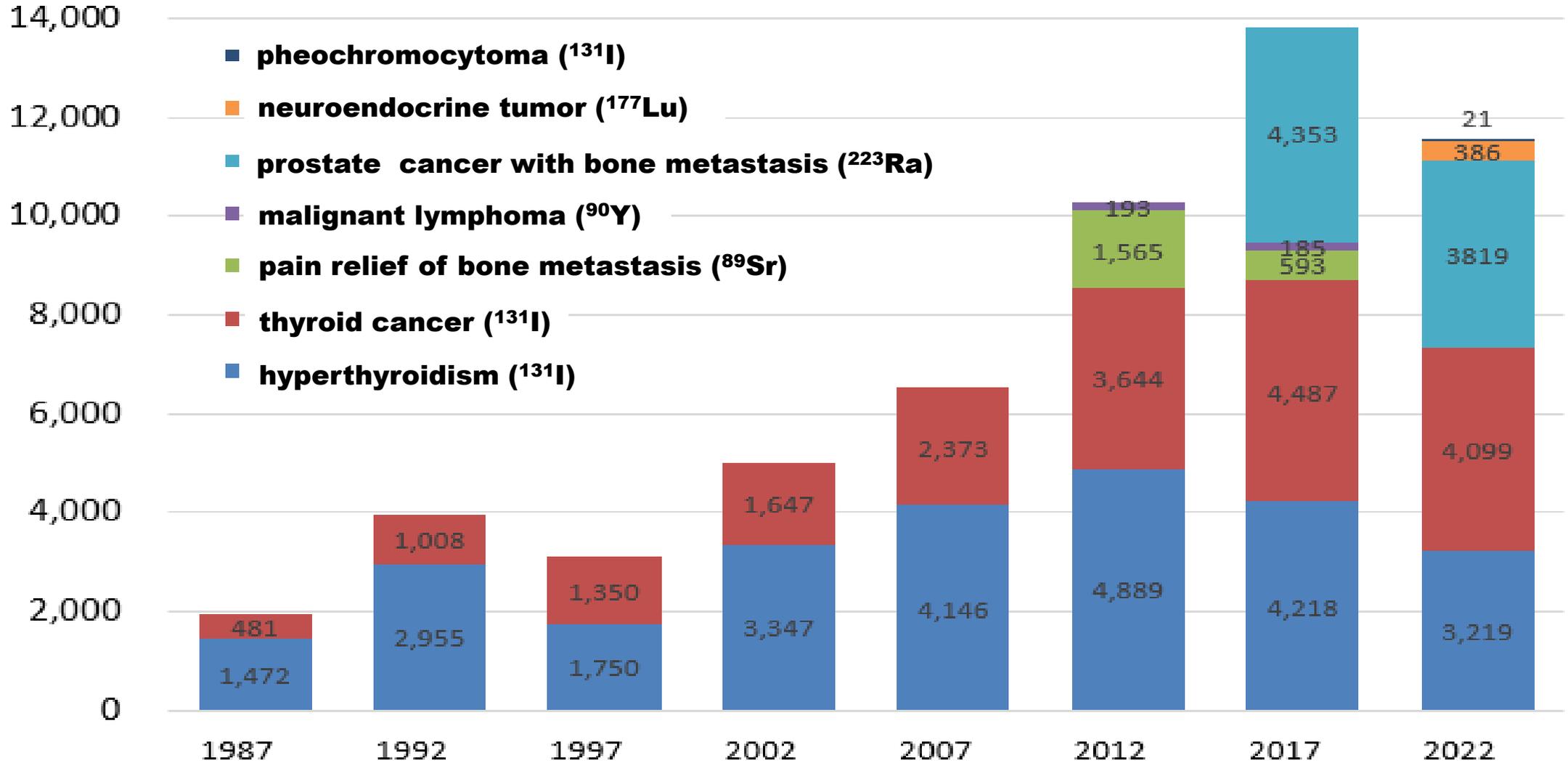


Number of PET tests (Estimated number of examinations in a year)

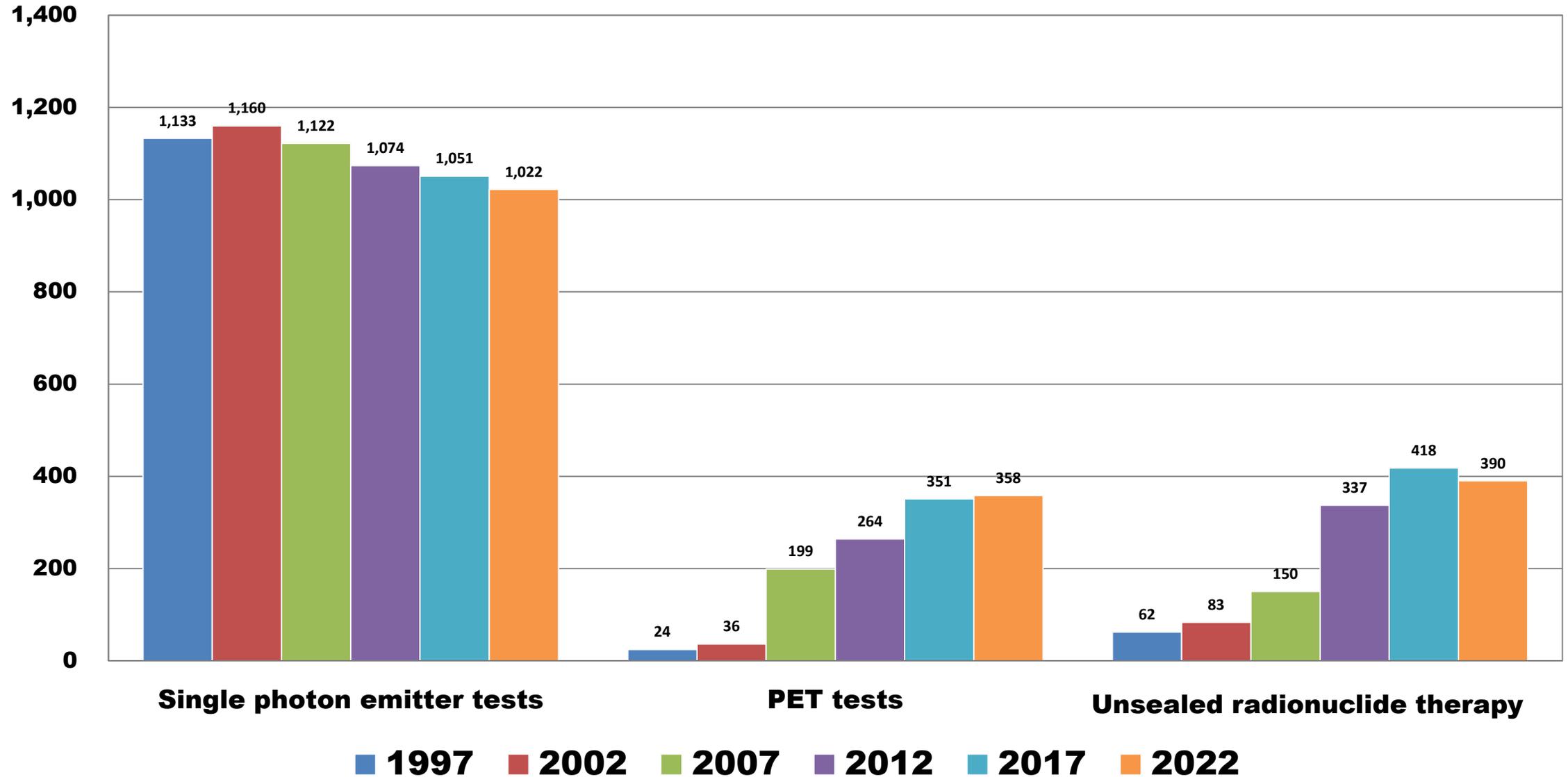


Annual Practice of Radioisotope Therapy in Japan

Annual practice

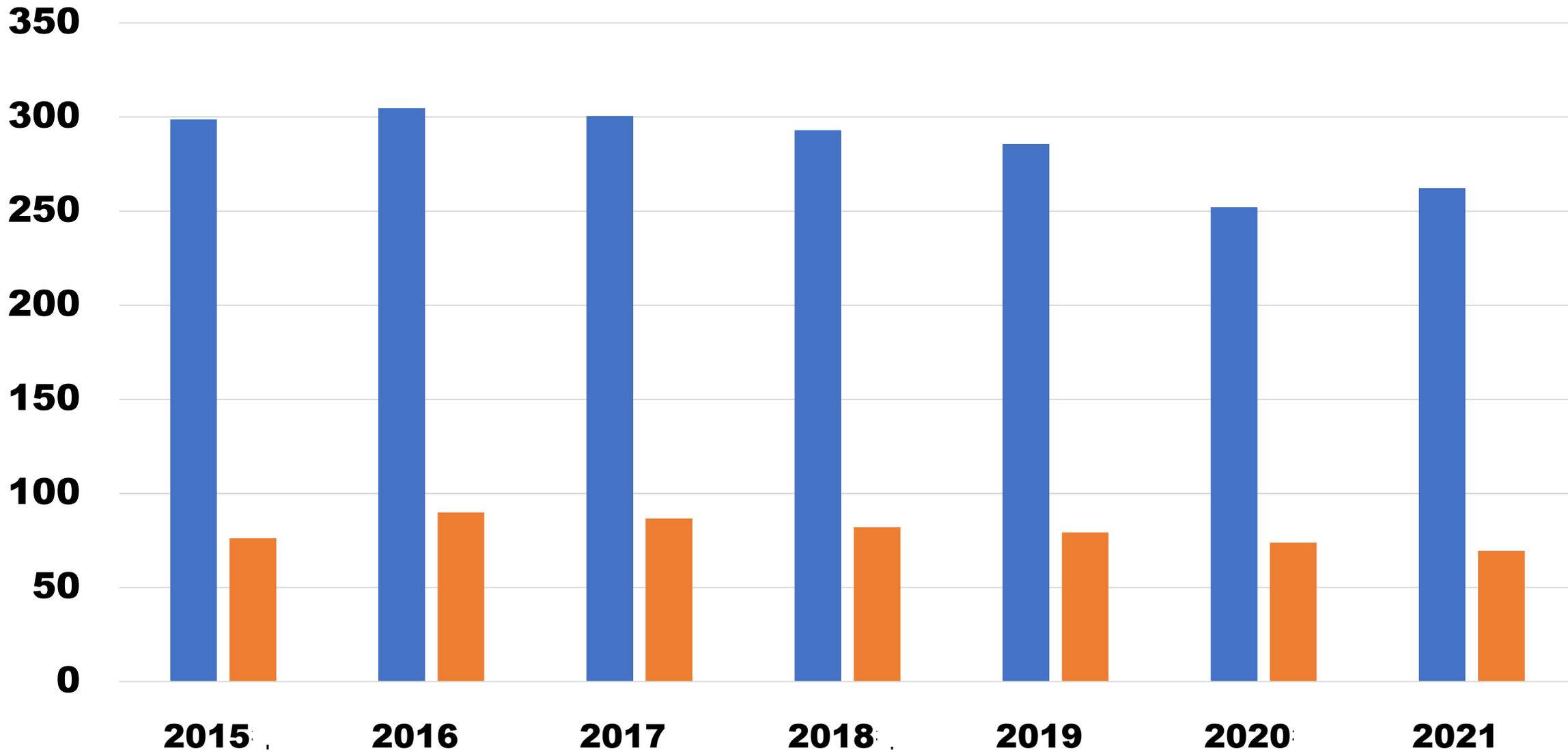


Institutions conducting nuclear medicine practice



(TBq)

Annual Use of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ in Japan



■ Tc-99m

■ Mo-99/Tc-99m

Japan Atomic Energy Commission
Japan Radioisotope Association

The Action Plan for Promotion of Production and Utilization of Medical Radioisotopes (Outline)

31st May, 2022 Atomic Energy Commission, Japan

Background

Expectations for Radioisotope Therapy

- Increased focus on *“theranostics”* (therapy + diagnosis)

Movements and Problems in Japan

- *Restart of research reactors* that can produce large amounts of radioisotopes (JRR-3, “Joyo”)
On the other hand, insufficient number of
 - *Hospital beds* for radioisotope therapy
 - *Human resources* who promote production and utilization of radioisotopes

International Situation

- *Vast investment* for radioisotope production and R&D
- Forming network of research reactors and accelerators
- Accelerated *competition for acquisition* of radioisotopes and their raw materials

Developing the Action Plan that aims to provide domestic radioisotopes to patients

The Action Plan contributes to

- Improvement of people’s welfare by enhancing the medical system through cutting-edge nuclear science and technology
- Ensuring economic security in terms of medical services

Goals to be Achieved during next decade

- ① Establishment of a Stable Radioisotope Diagnostic System through *partial domestic production of Mo-99/Tc-99m*
- ② Implementation of *Radioisotope Treatment Using Domestic Radioisotopes*
- ③ *Dissemination of Radioisotope Treatment* in Medical Setting
- ④ Making Radioisotope-Related Fields, centered on Medicine, as a *“Strength” of Japan*

Contents of the Action Plan

(1) Promoting Initiatives for Domestic Production and Stable Supply of “Important Radioisotopes”

- Stable supply of *Mo-99/Tc-99m* using JRR-3 and accelerators (Manufacturing approximately *30% of domestic demand* by the end of FY2027 as far as possible, and supply to domestic)
- Strengthening R&D for mass production of *Ac-225* using “Joyo” and accelerators (Production demonstration by FY2026 with “Joyo”)
- Strengthening efforts to commercialize *At-211* (Indicating usefulness as a pharmaceutical product by FY2028)

(2) Establishment of systems and structure to promote utilization of radioisotopes in medical setting

- Establishment of hospital rooms for radioisotope treatment (Average number of months to wait for radioisotope treatment: *3.8m (2018) → 2m (2030)*)
- Preparation for commercialization of new radiopharmaceuticals (Th-227, Ga-68)

(3) Promoting R&D Contributing to Domestic Production of Radioisotopes

- Technical development support for production by research reactors and accelerators
- Promotion of initiatives by the Fukushima International Research and Education Organization
- Establishment of systems of non-clinical studies of radiopharmaceuticals

(4) Strengthening Research Infrastructures, Human Resources, and Networks for Production and Utilization of Radioisotopes

- Strengthening Human Resources in the Field of R&D and Medical Setting
- Strengthening the Supply Chain in line with Domestic Production
- Study of Mechanisms for Waste Treatment and Disposal

Follow-up the Medical Radioisotope Action Plan in Japan

(1) Promoting Initiatives for Domestic Production and Stable Supply of “Important Radioisotopes”

< Molybdenum -99/Techneium-99m >

- JAEA has started development of production technology of (n,γ) reaction using JRR-3, and started cost evaluation for production. Development of chemical separation technology has been started.
- JRIA held a meeting with JAEA, JRPA, private companies, and ministries & agencies, and summarized issues related to manufacturing, and supply of medical radioisotopes.

< Actinium -225 >

- QST has already licensed out the technology for the production of Actinium-225 using an accelerator to a pharmaceutical company. Developed a hot laboratory dedicated to alpha-emitting radionuclides in a clean room at QST. Developed a trailer house type controlled area that is inexpensive and easy to expand nationwide, and obtained a license for Actinium-225 from the Nuclear Regulation Authority.

< Astatine -211 >

- Research Center for Nuclear Physics, Osaka Univ. established “The Supply Platform of Short-lived Radioisotopes” including Astatin-211 and started clinical trials for thyroid cancer in 2021.
- Advanced Clinical Research Center, Fukushima Medical Univ. conducted radiopharmaceuticals from production & synthesis to pre-clinical and clinical trials. Also it started clinical trials for malignant pheochromocytoma and neuroblastoma.

(2) Establishment of systems and structure to promote utilization of radioisotopes in medical setting

- NIHS is examining whether PET nuclides other than the four PET nuclides, such as Gallium-68, can be disposed of as normal waste in the same way as the 7-day rule.

(3) Promoting R&D Contributing to Domestic Production of Radioisotopes

- MEXT and AMED established a new R&D area to publicly invite research proposals related to medical radioisotopes.
- F-REI conducted research and analysis of research themes in the fields of radiation science and drug discovery medicine.
- AMED compiled a draft guideline for non-clinical studies of nuclear medicine therapeutics, aiming to finalize by the end of FY2023.

(4) Strengthening Research Infrastructures, Human Resources, and Networks for Production and Utilization of Radioisotopes

- MEXT included the learning objectives for radioisotopes in the curriculum for pharmacy education.
- MHLW revised its guidelines to strengthen the staffing of full-time radiology technologists at base hospitals for cancer treatment in Japan
- CAO’s event on Astatine 211 led to a preparatory meeting for the establishment of the World Astatine Community (WAC) in February 2023.
- MHLW is coordinating with the NRA on the rationalization of treatment and disposal methods for the disposal of radioactive contaminated materials for medical use.

Note: This follow-up is conducted in accordance with the Action Plan. This follow-up describes the progress made in FY2022.

Current Concerns

- $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ continues to be an major medical radioisotope in diagnostic imaging in oncology (bone metastasis), cardiology (ischemic heart disease), and neurology (cognitive impairment).
- Amount of radioisotope is decreasing because of increasing sensitivity of scanner and expanding PET use. However, it may increase globally due to an expansion in neurology in senile society to diagnose early Alzheimer disease.
- Needs of radioisotopes (^{225}Ac , ^{177}Lu , ^{211}A , and others) for cancer therapy is increasing because of application beyond traditional use for thyroid cancer.
- In planning domestic production and supply chain, the cost, standardization of quality, transportation, human resource development of nuclear medicine professionals, clinical trials for new radioisotopes, radioactive waste management, and safety and security system are major concerns in Japan.
- Under the action plan, realistic supply chain is now being investigated.