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EDITORIAL

EANM perspectives for CZT SPECT in brain applications

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CZT SPECT systems have deeply changed the practice of cardiac imaging [1]. Regarding neuroimaging, although no dedicated CZT SPECT system exist for the brain and that PET imaging remains the high standard for molecular brain imaging, the practice is worldwide emerging with more than one hundred CZT 3D SPECT systems already installed. This Editorial will discuss the current available standard for brain applications on CZT SPECT systems and present the perspectives that can be expected from these systems for nuclear neurology, based on review of the literature combining the terms ("CZT" OR "Cadmium-Zinc-Telluride") AND ("brain" OR "cerebral") in Pubmed database.

CZT SPECT systems and advantages for brain applications

CZT-based detectors were first proposed for SPECT imaging over twenty years ago [2]. The key advantage of CZT detectors over traditional scintillation crystals are a semiconductor material composed of cadmium-zinctelluride, capable of directly converting gamma photons into a flow of charge, bypassing the process of optical light emission and detection. This translates into higher contrast and energy resolution, and to a lesser extent a higher spatial resolution, for any volume of interest including brain SPECT imaging. Currently available CZT SPECT systems use pixelated detectors in 2D CZT-cameras (2 flat detectors) and 3D CZT-cameras (12 detectors over 360°) for which a focused acquisition can be performed on a specific volume of interest such as the brain. Preliminary studies in brain SPECT with 2D CZT-cameras were conducted over a decade ago,

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demonstrating its capability to reduce both injected activity and acquisition time without compromising image quality [3]. These findings were then supported through comprehensive and rigorous clinical studies, confirming its capability to reduce the acquisition time of brain SPECT studies by half [4]. Regarding the 3D CZT-cameras, a first head-to-head comparison between a prototype SPECT system and a conventional camera was conducted in 35 patients, including five brain studies, showing qualitative improvement in contrast and image quality [5]. Furthermore, phantoms studies on commercial 3D CZT-cameras, confirmed higher sensitivity and energy resolution compared to conventional cameras (from 9.2 to 5.5%) [6] giving also the possibility to perform multi-tracer studies. These remarkable advantages were translated into clinical routine in terms of brain perfusion and dopaminergic imaging showing concordant SPECT results when compared with a conventional camera, but with shorter acquisition times, limiting movements during the acquisitions, and higher image quality [7, 8]. Furthermore, the high-count sensitivity of CZT cameras and ultimately their capacity to provide fast whole-body recordings with suitable image quality makes the technique particularly interesting for theranostics, a concept integrating molecular imaging and targeted radionuclide therapy for personalized cancer therapy [9]. Other novel properties of CZT cameras including dynamic imaging and quantification are at their infancy in brain applications and should be further explored in the future.

CZT SPECT in brain perfusion

Brain perfusion SPECT, utilizing ^{99m}Tc-labeled radiopharmaceuticals like ECD or HMPAO with CZT detectors, offers several notable advantages over classical Anger acquisitions, especially for 3D CZT-cameras [7, 10–12]. In particular, there's the potential for simultaneous acquisitions of ^{99m}Tc- and ^{123}I-labeled radiopharmaceuticals for perfusion and dopaminergic neurotransmission in atypical parkinsonian syndromes [11]. The improved temporal resolution, coupled with enhanced sensitivity, also facilitates the research development of dynamic brain connectivity studies [13].

Brain perfusion SPECT provides advantages as compared to imaging of glucose metabolism using [^{18}F]FDG albeit competitive advantages of PET instrumentation. Pertinent conditions for brain perfusion SPECT imaging may include:

- Brain activation studies in research particularly in psychiatry [14, 15], and clinical settings such as ictal and interictal imaging in focal epilepsy [16], including stimulation studies in patients implanted with stereo-electro-encephalography [17]. This consideration takes into account the faster uptake of ^{99m}Tc-radiopharmaceuticals for perfusion compared to [^{18}F]FDG and the practicality of being able to administer the radiopharmaceutical during a seizure and imaging later [18, 19],
- Studies of vascular reserve after acetazolamide in patients with carotid stenosis or vasculopathy (e.g., Moya-Moya disease), with the potential for increased sensitivity to conduct rest- and test-acquisitions on the same day [19, 20],
- Brain imaging of psychiatric diseases where an uncoupling of cerebral blood flow and glucose metabolism has been observed, particularly in unipolar patients [21–24]. This phenomenon is positively correlated with disease severity, characterized by a greater reduction in cerebral blood flow compared to cerebral metabolic rate of glucose [21], and is also associated with post-therapeutic changes [23],
- Limited availability of PET imaging and patients with uncontrolled diabetes and hyperglycemia as relative indications [18].

CZT SPECT in dopaminergic imaging

One of the primary areas of interest for CZT and 3D CZT-cameras lies in the qualitative evaluation and semi-quantification of presynaptic receptor occupancy (mainly employing [^{123}I]-Ioflupane) owing to the potentially heightened sensitivity and spatial resolution. In literature, studies investigated large 2D CZT-systems [4, 25–27] and 3D CZT-systems [8, 28–30] focusing on scanner geometries ([29] and [30] from the same group) or collimators [25].

From a clinical standpoint, it has been demonstrated [4] that there is a twofold reduction in scan time for [^{123}I]FP-CIT ([^{123}I]Ioflupane) and even greater efficiency for 3D CZT-systems compared with 2D CZT-cameras due to a + 25% increase [8] in tomographic count sensitivities (when using focus acquisition) as well as significantly higher quality scores and increased spatial resolution. Finally, a pharmacological study [28] utilizing a 3D CZT-camera confirmed that striatum/occipital ratio was significantly influenced by specific serotonergic antidepressants. An issue that emerges is the concern that commonly used, or commercially available "normal databases" may not be compatible with such distinct geometries, reconstruction algorithms especially with 3D systems, resolution and sensitivities. While it has been observed that signal-to-background ratio (SBR) values from visually normal scans do not significantly deviate from existing reference databases with 2D CZT-cameras [26], others [27] have noted that, a CZT-dedicated database could lead to fewer discrepant ratings between semi-quantification and visual analysis in pathological case studies. An international effort to collect a substantial number of [^{123}I]Ioflupane cases to develop robust 2D-CZT and 3D-CZT databases is imperative. Moreover, a harmonization process is necessary concerning acquisition and reconstruction parameters.

CZT SPECT for theranostics of brain tumors

With the recent advances of radionuclide therapy in neuroendocrine tumors and prostate cancers, there is an increasing interest in theranostics applications, including brain tumors [31]. The theranostics concept with SPECT imaging in neurooncology is characterized by the possibility of an individual assessment of tumor heterogeneity, a dosimetry estimation, and a treatment monitoring response. These radionuclide therapies are currently mainly performed using Lutetium-177 (^{177}Lu) as the radionuclide, which allows both therapy and SPECT post-treatment imaging based on its dual β and γ emission.

A number of studies have used SPECT imaging after radionuclide therapy of brain tumors to assess the distribution of radiotracer uptake and perform tumor dosimetry [32–38]. Performing internal dosimetry both in tumor and critical organs is required by current EU regulations [39] with recent efforts from the European Association of Nuclear Medicine (EANM) to develop its widespread clinical application and standardization [40].

A pilot study compared detectability of lesions from different tumors post-therapy in patients treated with ^{177}Lu-labeled radiopharmaceuticals using both conventional and 3D CZT-cameras systems [41]. CZT SPECT system post-therapy scans, acquired with faster scanning time, demonstrated larger lesion detection and had comparable detection/targeting rate compared to conventional SPECT/CT systems [41]. Moreover, if absolute quantification of ^{177}Lu is feasible with conventional cameras [42], this has also been reported recently for 3D CZT-cameras [43, 44]. In routine, 3D CZT-systems allow acquisition in a limited time, whole-body SPECT imaging with an accurate quantification of ^{177}Lu-radiopharmaceutical uptake for both assessment of tumor heterogeneity and dosimetry calculation [38]. The preliminary results of radionuclide therapy treatment monitoring with 3D-CZT SPECT systems reported for [^{177}Lu]Lu-PSMA in prostate cancers [45] open the way for an analogous use for brain tumors.

One of the most advanced clinical applications of radionuclide therapy in brain tumors is based on targeting somatostatin receptors in meningiomas with encouraging results in term of progression free survivals [46]. Ideally, SPECT imaging acquisitions for [^{177}Lu]Lu-DOTATATE (or somatostatin receptor targeting analogues) in meningiomas are performed with at least 3 time points, starting 1–4 h up the day 7 after therapy administration for dosimetry calculation [47]. Acquisitions with multiple timepoints further emphasize the importance of fast acquisition protocols.

Conclusion and perspectives

The advantages of the CZT SPECT technology in terms of contrast and energy resolution are of specific interest in perfusion and dopaminergic imaging as well as theranostics. From the currently available data we can draw the conclusion that CZT SPECT acquisitions provide at least comparable image quality as conventional systems but with shorter acquisition time, thus associated with an advantage in workflow management and patient acceptance. Current efforts are ongoing for the standardization of protocols across centers and vendors, to provide updated reference data compatible with this novel technology and to explore comprehensively the ability of this new technique to further improve diagnostic accuracy and patient management.

Declarations

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Informed consent Not applicable.

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