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Against

Yes and no. The answer is *yes* if the question is interpreted as whether or not LSO will be an important scintillator for positron emission tomography (PET) scanners in the future. The answer is *no* if the question is interpreted as whether or not LSO will be the *only* scintillator for PET scanners in the future.

LSO improves the performance of 3-D PET

Certainly lutetium oxyorthosilicate (LSO) has drawn considerable attention since it was first reported on by Melcher and Schweitzer [1] in 1992. It has a very favorable combination of properties for PET imaging compared with the other scintillators then (and still) in use in PET, namely bismuth germanate (BGO) and sodium iodide (NaI) (Table 1). LSO was first used in the microPET animal scanner from UCLA [2] and the research brain HRRT scanner from Siemens/CTI [3], but it was only in 2001 that LSO was offered in a commercial whole-body scanner intended for clinical use – the Siemens/CTI Accel.

The advantages of LSO are best appreciated for 3-D imaging without septa. For 2-D imaging with septa it is hard to beat BGO, since it has the highest stopping power of all scintillators commonly used in PET. The low light output of BGO leads to poor energy resolution, but this is relatively unimportant in 2-D PET since the septa limit scatter and randoms. The advantage of 3-D imaging is the large gain in true sensitivity, but this is partially offset by a gain in scatter and random coincidences, both of which decrease contrast, often leading to decreased lesion detectability in fluorine-18 fluorodeoxyglucose (FDG) studies. A common way to evaluate the trade-off of signal (true coincidences) vs noise (scatter and randoms) is to measure the noise-equivalent count rate (NEC) [4]. The NEC accounts for the additional noise that scatter and randoms contribute to the image, even though correction methods are used to compensate for the bias from scatter and randoms. In comparisons using BGO scanners with retractable septa, the NEC is higher in 3-D (septa out) for small activity distributions [5] such as those encountered in brain studies, but the gain is modest for whole-body studies, since scatter and randoms increase and there is unshielded activity from outside the field of view (FOV). In fact, comparisons of patient studies using BGO scanners indicate better image quality for 2-D for whole-body oncologic studies [6]. But, BGO is definitely not the best scintillator for 3-D. 3-D PET demands a fast scintillator to reduce dead time and randoms, and one that has good energy resolution to reduce scatter and randoms from inside *and* outside the FOV. In both speed and energy resolution, LSO has a clear advantage over BGO, and the NEC for the Accel in 3-D [Dr. M. Casey, personal communication] – as measured with the 70-cm-long phantom [7] which is relevant for whole-body studies – is higher than the EXACT, which is very similar in overall design, but which uses BGO instead of LSO. In clinical practice, the Accel scanner performs well in 3-D for both brain and whole-body studies.

GSO as an alternative to LSO

The Allegro scanner introduced in 2001 by Philips Medical Systems uses gadolinium oxyorthosilicate (GSO), an alternative to LSO. The GSO Allegro operates exclusive-

Table 1. Comparison of properties for scintillators currently used in PET. Energy resolution measured at 662 keV for a single crystal coupled to a single PMT; thus the measured value does not include effects of detector design. Data from [10] and [11]

Scintillator	NaI(Tl)	BGO	GSO	LSO	LuAP	LPS	LaBr
τ (ns)	230	300	60	40	18	30	35
μ (cm^{-1})	0.35	0.95	0.70	0.86	0.95	0.70	0.47
ΔE/E (%)	6.6	10.2	8.5	10.0	~15	~10	2.9
Rel. light output (%)	100	15	25	70	30	73	150

ly in 3-D, and achieves a true coincidence rate of about 70–80 kcps for typical FDG whole-body studies – very competitive with the LSO Accel. In comparison, a BGO scanner in 2-D mode acquires a true coincidence rate of about 20–25 kcps. For both the GSO Allegro and LSO Accel the higher count rate in 3-D can be translated into higher image quality *and* shorter imaging time. For these 3-D systems the total acquisition time recommended for a whole-body study is 30 min or less, compared with about 1 h for 2-D BGO systems.

GSO is not a new scintillator; in fact, it was developed in 1983 [8] and had been used (alongside BGO crystals) in a 2-D PET scanner by the Karolinska group [9]. The interest in GSO for PET applications dropped off quickly in the 1980s in favor of BGO, since for 2-D PET stopping power is most important, rather than decay time and energy resolution. As seen in Table 1, LSO has higher stopping power and faster decay than GSO, which are clear benefits. LSO also has higher light output than GSO, but the intrinsic non-proportionality of LSO leads to poorer energy resolution [10]. Note that the values of scintillator energy resolution listed in Table 1 can be used for comparison, but are not representative of the system energy resolution of PET scanners based on these scintillators. System energy resolution also depends on detector design and the accuracy of system-wide calibrations. Better energy resolution is important, particularly in 3-D PET, as it allows the scanner to be operated with a higher energy threshold E_{thresh} closer to 511 keV in order to reduce scatter and random coincidences without reducing true coincidences. The overall system energy resolution of the GSO Allegro scanner is 15% and the E_{thresh} is set at 420 keV. In comparison, the E_{thresh} for the LSO Accel is 350 keV, similar to that of the BGO scanners, which typically have an energy resolution of about 20%. Regardless of scintillator, a lower E_{thresh} leads to a higher scatter fraction. On the other hand, the good timing resolution of LSO allows the coincidence timing window to be reduced to 6 ns, which is effective in reducing random coincidences, also important for 3-D PET. This can be compared to a timing window of 8 ns for GSO and 12 ns for BGO scanners.

Another important property of GSO is the consistency of light output, which is due to improvements in production made recently by Hitachi Chemical [12]. Measurements that we have taken with GSO demonstrate that the light output variation among thousands of crystals is only 7% (SD). In comparison, there have been inconsistencies of production of LSO, in both decay time and light output – variations as large as a factor of 3 in light output have been reported [13, 14]. Another advantage of GSO is that it is not radioactive. Although the radioactive decay of LSO does not interfere with coincidence detection of 511-keV annihilation photons, it does make it more difficult to use singles transmission scanning. For 3-D PET, singles transmission [15] has been shown to be a very cost-effective and fast method of acquiring transmission data for attenuation correction. For Allegro, a single cesium-137 point source (662-keV gammas) is used to acquire transmission scans for each bed position in about 40 s.

Unfortunately, both LSO and GSO suffer the drawback of high cost – at least a factor of 5–10 higher than NaI and a factor of 3–6 higher than BGO. As production capacity increases, it is possible that LSO and GSO will become less expensive, perhaps as other manufacturers make production of these scintillators more competitive. Nevertheless, it is unlikely that either LSO or GSO will reach the low cost of NaI and BGO owing to the much higher melting point (>2,000°C) and difficulty in growing large boules.

Detector design is as important as choice of scintillator

It is important to recognize that the performance of a PET detector depends not only on the properties of the scintillator, but on the detector design itself. The goal of the detector design is to clearly identify crystal position and to preserve the intrinsic energy resolution of the scintillator. The GSO detectors used in the Allegro scanner incorporate discrete crystals but with continuous optical coupling through a light-guide. The Anger-logic detector resolves 4-mm crystals with a hexagonal array of 39-mm photomultipler tubes (PMTs) [16]. For each event a local cluster of seven PMTs is used to determine position and energy.

The GSO detector design differs from block detectors [17] in that the light-guide for the GSO detector is continuous and there is no particular alignment between crystals and PMTs. The detector for the GSO brain scanner (G-PET) uses a single annular light-guide [18], whereas the whole-body Allegro scanner with a larger diameter uses 28 modular detectors, optically coupled together. The intrinsic advantage of the continuous light-guide with a close-packed array of PMTs is that the variation in light collection from different crystals in the detector is minimized, thus leading to good system energy resolution. For the GSO detector the light collection varies by at most 20% (between center of PMT and edge of PMT), whereas a block detector can have as much as a factor of 3 difference in light collection (between center of PMT and edge of block) [19]. The large variation in light collection in the block detector is a result of the cuts in the crystal block (or light-guide) which are designed to achieve good crystal identification with a scintillator such as BGO that has poor light output. Even though LSO has higher light output and better energy resolution than BGO, the block design may be limiting the system energy resolution.

Another difference between the GSO detector and block detector designs is the crystal-to-PMT encoding ratio. The encoding ratio of the GSO detector is about a

factor of 4 higher than the detector blocks used in both the BGO EXACT and the LSO Accel, which resolve an 8×8 array of 6.4-mm crystals with four 25-mm PMTs. In general, a higher encoding ratio is more favorable, as it leads to a reduced number of PMTs, and thus lower system cost. The trade-off is that a higher encoding ratio may result in increased dead time, but the advantage of fast decay time for GSO (and LSO) is that the pulse integration period can be reduced by a factor of 6 compared with BGO, thereby reducing dead time.

A variant of the block detector is the quadrant sharing design developed by Wong [20] and used in the MD Anderson PET scanner [21]. This design has a more favorable encoding ratio than the conventional block detector; thus it can resolve smaller crystals for a given PMT size. However, the quadrant sharing design has higher dead time since a larger number of PMTs, nine vs four, are involved in positioning each event. Recent reports of the new LSO panel detectors [22], which resolve 4-mm crystals with 50-mm PMTs in a quadrant sharing block design, suggest that better energy resolution, about 12%, is measured, but an E_{thresh} of 350 keV continues to be used. To take advantage of the better energy resolution, the E_{thresh} needs to be raised.

The future of 3-D PET

Although excellent image quality is achieved with both the GSO Allegro scanner and the LSO Accel scanner, there continues to be a drive toward improved scanner performance. There has been considerable research and development of inorganic scintillators for PET imaging over the past several decades (see [11] and references therein) and the search for the ideal scintillator seems to be intensifying. Both GSO and LSO were introduced into clinical whole-body 3-D PET scanners for the first time in 2001, yet GSO is close to 20 years old, and LSO is close to 10 years old. What's on the horizon?

The application for PET typically focuses on scintillators that have very high stopping power. There are several manufacturers who currently produce small quantities of scintillators similar to LSO; this includes MLS (mixed lutetium silicate) from UTAR, Canada and LGSO (90% lutetium and 10% gadolinium) from Hitachi, Japan. Other examples of new scintillators include LuAP (lutetium aluminum perovskite) and LPS (lutetium pyro-silicate) [11]. As shown in Table 1, LuAP has higher stopping power than LSO, faster decay, but lower light output – and worse energy resolution. LPS has similar stopping power as GSO, faster decay, and higher light output – but worse energy resolution. Both are promising, but neither is ready for full-scale production. A very interesting class of lanthanum scintillators, LaCl and LaBr [23], is being developed by Saint-Gobain Crystals and Detectors. The decay time of the lanthanum scintillators is fast, and the energy resolution is outstanding, about 3%. Although the stopping power of LaBr is lower than GSO, we have shown that 3-D PET is not limited so much by its sensitivity, but rather by its count rate capability and ability to reject scatter and randoms. Clearly, the lanthanum scintillators would have very high count rate capability through use of a very short pulse integration time (≤100 ns) and excellent rejection of scatter and randoms, through use of a high E_{thresh} (≥470 keV) and narrow timing window (≤6 ns). Also, due to the very high light output, one could achieve excellent spatial resolution with narrow (but thick) crystals in a detector design similar to that of the GSO detector.

The significance of a scintillator such as LaBr is that it can potentially move us in a direction of increasing PET performance, without driving up the cost of the instrument. Although there is certainly a high cost of developing new technology, the long-term cost of the lanthanum scintillators is not expected to be high, since the melting point is relatively low, about 800°C. It is the high melting point of GSO and lutetium-based scintillators that makes these scintillators so costly, which constitutes a large fraction of the total cost of the PET scanner.

Summary

The performance of a PET instrument depends on many aspects of design and data processing, in addition to the scintillator choice and detector design, which is the focus of this article. In particular, for 3-D PET the combination of accurate attenuation correction and a fully 3-D iterative reconstruction algorithm have been shown to have a very significant impact on image quality [24]. A major goal in clinical FDG imaging is to optimize image quality in order to improve lesion detectability. Although it is a difficult measure to quantify, lesion detectability requires high signal and low noise – and thus, high true coincidence counts and low scatter and random coincidences. High spatial resolution is important, as well, to ensure that the true events are placed in the correct location. In fact, one drawback of the Accel (and EXACT) is that spatial resolution is close to 6 mm, whereas the spatial resolution is less than 5 mm for the Allegro. For 3-D PET there is a huge potential for improved performance, which depends on a complex combination of scintillator properties, including stopping power, decay time, and energy resolution. The key is to increase the true coincidence rate while limiting the scatter and random coincidences. This requires good energy resolution of the scintillator and of the detector design so that the energy threshold can be raised close to the photo-peak energy. This is particularly important for heavy patients who have increased attenuation, which causes true coincidences to decrease as scatter increases. Today's 3-D instruments with both LSO and GSO already have the capability of superior performance to 2-D PET for clinical FDG studies. The increased count rate performance

should be used to attain higher image quality and improved lesion detectability, not just shorter imaging time. Is there room for improvement in the future with new scintillators already under development? I believe so.

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