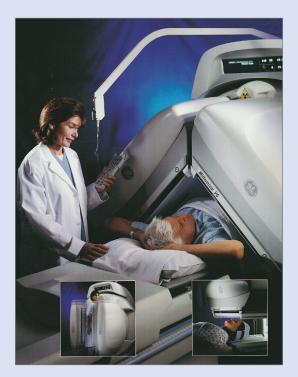
# Celebrating 20 Years of SPECT/CT

The introduction of Hawkeye, the world's first hybrid imaging system

Nearly 20 years ago, a pivotal event shaped the future of nuclear medicine. Once called the "unclear medicine," nuclear medicine was forever changed with the introduction of Hawkeye, the world's first clinical hybrid imaging system. GE Healthcare (at that time known as GE Medical Systems) introduced Hawkeye, a dual-modality SPECT and CT system, at the 1999 Society of Nuclear Medicine (SNM) Annual Meeting, heralding in a new era of "more clear medicine."



**Figure 1.** Hawkeye combined a Millenium VG camera with an X-ray tube and detector that rotated around the patient.

### The unclear medicine

Invented by Hal O. Anger in the mid-1950s, nuclear medicine cameras detect gamma radiation to depict metabolic processes within a living body. While gamma cameras helped revolutionize the field of functional medical imaging, there was one key limitation: the lack of anatomical markers in the image.

"We always understood that we needed anatomical and structural data to provide the best details and a precise answer to the clinical question," says Ora Israel, MD, Director Emeritus of Nuclear Medicine/PET (retired) at Rambam Healthcare Campus, Haifa, Israel. She recalls using fiducial markers placed on the patient's body to identify the location of key anatomical areas, such as the chest or abdomen.

In some cases, Professor Israel and her colleagues would try to repeat the nuclear medicine study on a CT with the patient in the same position. It was a difficult and time-consuming process that she says never really worked well.

"There was a clear purpose to improve the specificity of nuclear medicine by defining the anatomical relationship between isotope imaging and anatomy," says Martin Sandler, MD, Professor of Radiology and Radiological Sciences and formerly Chairman of the Department of Radiology and Radiological Sciences at Vanderbilt University School of Medicine.

Although fusion software was being utilized in some institutions, the applications were limited. "The brain was fairly simple, but the key problems came in the abdomen as a result of respiratory motion," Dr. Sandler explains.

This key clinical challenge in nuclear medicine was also shared with Elscint, and later ELGEMS, a joint venture between Elscint

At the moment we saw the first images, there was an understanding of the power of this new modality. Professor Ora Israel HAWKEYE

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and GE Medical Systems (now GE Healthcare) to develop gamma camera technology. According to Nathan Hermony, VP Nuclear Medicine Business, the company started to look at the issues surrounding nuclear medicine, primarily the "unclear medicine."

"The perception of nuclear medicine being the 'unclear medicine' was one of the key issues in the specialty," Hermony says. "Referrers couldn't understand what they were looking at. So we asked our medical advisory board, what can we do to improve this?"

For the non-nuclear medicine physician who was often treating the patient, using the information from gamma cameras could be a very frustrating process. James A. Patton, PhD, DABR, Professor of Radiology and Program Director of Nuclear Medicine Technology, Vanderbilt University Medical Center, recalls watching nuclear medicine physicians examining X-rays and CT images to try and discern where the hot spot was at anatomically in the nuclear medicine study.

"It was also very difficult to convey to the clinicians exactly what diagnostic information had been identified for them; all they would see was this glob representing abnormal radiopharmaceutical uptake," he explains. In fact, Dr. Patton spent hours trying to put together functional and anatomical maps that clinicians could use as guidance when reviewing nuclear medicine images, first using ultrasound and then CT after it was commercially introduced.

Then, in the early-1990s, a new concept began to emerge. Timothy G. Turkington, PhD, Associate Professor of Radiology and Faculty Member in Medical Physics at Duke University, recalls attending a presentation at an IEEE Medical Imaging Conference given by the research group of Bruce Hasegawa, PhD, from the Radiology Department at the University of California, San Francisco (UCSF).

"They presented their work on a combined SPECT and CT system," Dr. Turkington says. "To me, it seemed very complicated and I didn't really get the point. Also, their system included fairly old technology for both SPECT and CT. I thought 'why do this if both systems will be updated' (over time). But, when you put these two modalities together, you actually get more than the sum of the two. Bruce saw this from the beginning."

Dr. Hasegawa is best known for his pioneering work on multimodality imaging, combining CT with SPECT to provide an

overlay of radiotracer functional distribution on an anatomic image. According to a biography in the Journal of Nuclear Medicine, he borrowed equipment from GE and placed a single-head SPECT camera close to a CT ring and then took sequential scans using the same patient bed. Dr. Hasegawa also developed the algorithms to co-register the two images.<sup>1</sup>

Dr. Patton recalls Dr. Hasegawa as the "ultimate gentleman and researcher. I wanted to use his bilinear model and figure in a publication, so I emailed him for a formal release. He emailed me back with permission to use anything in any article he had ever published. Unfortunately, he passed away a few months after that."

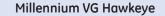
#### **Overcoming challenges**

While CT could certainly address the issue of anatomical markers in nuclear medicine, there were other challenges that it could resolve as well. Dr. Turkington had worked as a postdoc with Ronald J. Jaszczak, who at that time was Professor in the Department of Radiology at Duke, on improving quantitative SPECT imaging.

"A key component of quantitative SPECT is attenuation correction," Dr. Turkington explains. "To do that, you need information about the body. The methods to obtain this information were fairly complicated using radioactive sources and they weren't widespread. Using X-ray CT to get the same information was a newer concept that Bruce and others were working on. In addition to enabling quantification, attenuation correction makes the SPECT images more qualitatively appealing, as well."

In the mid 1990s, Duke was performing several PET brain studies on cancer patients each day. They routinely used a contrast-enhanced T1 MR image, which revealed breakdown of the blood brain barrier, registered with the patient's PET brain image, which provided more specific information about the abnormalities. While there was rigidity and enough common features in the brain to fuse MR and PET, in the body it was much more challenging to provide this retrospective registration, whether the modalities were PET, SPECT, MR or CT.

Gadolinium was also being used to provide attenuation correction for nuclear cardiology studies. However, it was a time consuming procedure, not a fail-proof solution, and didn't always provide the information needed.



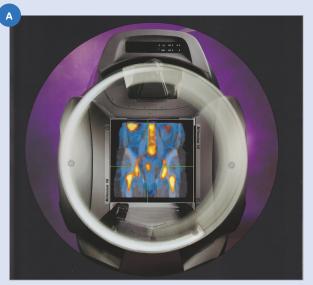


Figure 2. GE Healthcare print advertising depicting some of the first clinical images obtained from the Hawkeye systems. (B) The Millennium VG5 Hawkeye was capable of PET Coincidence Imaging (CoDe™), as shown in the clinical image.

"The idea of moving from gadolinium to CT came up as a more precise way to achieve attenuation correction in cardiology studies," Professor Israel explains. "At the same time, we were trying to explain to our colleagues at Elscint and then ELGEMS that we needed an easier way to facilitate the fusion of functional and anatomical data."

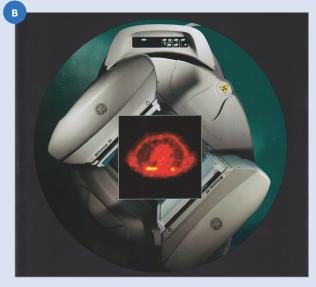
#### A vision for the future of nuclear medicine

While Dr. Hasegawa is widely considered the pioneer of multimodality functional-anatomic imaging, several others were following his lead and working on the development of a commercially available SPECT/CT system. The formation of ELGEMS in 1997 further propelled this effort. At the time, the companies said by pooling their R&D capabilities their financial prospects in nuclear medicine could be enhanced. Elscint wavered at 10% market share while GE looked to enhance its variable-angle, dual-head camera product line. The partnership would be a win for both organizations.

GE moved its manufacturing and R&D operations to Elscint in Haifa, Israel, where the nuclear division remains today. Elscint veteran Hermony was tapped as President and CEO of ELGEMS; today, he remains at the helm of GE Healthcare's Nuclear Medicine business.

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#### Millennium VG5 Hawkeye



"Our primary goal was to examine the underlying issue of nuclear medicine being the 'unclear medicine' and change that perception," Hermony says. "Clearly, this was one of the primary reasons we pursued hybrid imaging. The other was attenuation correction. So, we believed that combining an X-ray source, such as CT, could correct for the attenuation in the body and also localize the activity within the patient's anatomy so physicians could see where that lesion was at."

By bringing together anatomical with functional imaging in a single hybrid system, the team at ELGEMS was in pursuit of improving image quality, attenuation and lesion localization in nuclear medicine. According to Hermony, fusing the imaging data from two separately acquired exams was fraught with the potential for error and suboptimal results.

"If the nuclear medicine image is unclear with no body contour, no algorithm can register the images from two different systems acquired separately," Hermony says. "That point was clear when we developed Hawkeye and it remains so today."

Although ELGEMS had several clinical-academic relationships, it was the collaboration with Vanderbilt University, Duke University and Rambam that propelled the development of hybrid SPECT/CT. At that time, R. Edward Coleman, MD, Professor of Radiology and Director of Nuclear Medicine, was leading the effort at Duke. SPECT/CT

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"Dr. Coleman was always interested in new technology," Dr. Turkington adds. "Some people are just oriented in looking for utility in new things, and he was one of them. If Dr. Coleman thought something could improve patient care, he was very encouraging. And he was mostly positive about this concept."

As part of a medical advisory board (MAB) to ELGEMS, Drs. Coleman, Turkington, Sandler, Patton, Israel and Dov Front, who at that time was the Director of Nuclear Medicine/PET at Rambam, met in Haifa in early 1997 to discuss new updates to gamma cameras, emerging concepts and options for the future. The Haifa team discussed making Dr. Hasegawa's concept into a product using a low-power X-ray tube and detector on their SPECT gantry, which already had slip-ring capability. This would be a relatively inexpensive add-on.

"That was probably the best part of this project, to sit down with all these bright minds and brainstorm the future," Dr. Patton recalls. "We were given a security clearance on what ELGEMS was envisioning. We had little pieces of paper with questions; if we had all options available, how would we approach functional anatomical imaging. I think it was the most fun I've had in my career."

And that is where the concept for Hawkeye, the world's first commercially available SPECT/CT hybrid system, came to fruition. The company's gamma camera, Helix (followed by the Varicam and VG), had slip ring technology that the ELGEMS development team believed would facilitate the addition of a CT on the same gantry.



Figure 3. Depiction of the table and camera motion.

Yet, even if ELGEMS could get the system to work, many questions arose and the engineering team needed guidance from its MAB. Would such as system even be utilized? How useful could it be in clinical practice? What barriers existed? Who would operate it?

Dr. Turkington recalls that the term "CT" was avoided in the first product. It was referred to as "anatomical mapping" for multiple reasons, among which was that the slowly rotating SPECT gantry (at the time it was a 14 sec rotation) could not produce the quality images of current CT scanners and would disappoint those expecting diagnostic CT quality. Allowing for attenuation correction and providing help in localizing SPECT lesions seemed enough, however.

Professor Israel remembers these meetings as fruitful discussions that benefitted all involved—the clinicians, physicists, engineers and scientists.

"An idea like Hawkeye could not have come from one side, only; we needed to collaborate from both sides—academia and industry," Professor Israel explains. "They listened to our requests and understood what we needed. There were available tools that the engineers thought might be useful for what we were asking for, as well. It was always a collaborative environment, very fruitful, a win-win situation for both sides.

"By sharing our frustration of not being able to co-register data obtained from separately performed tests, we helped envision and initiate development of the Hawkeye," she adds. All of this happened, she recalls, without really knowing what they were getting involved in.

In fact, it was the use of gadolinium for attenuation correction in nuclear cardiology studies that propelled the ELGEMS concept for Hawkeye. It became clear that the Gd AC map provided some anatomical references, creating a "Eureka" moment that inspired the pursuit of a hybrid SPECT/CT.

After the initial meeting in Haifa, the same team reconvened in Glasgow at a small MAB meeting prior to EANM 1997. From that point forward, Dr. Turkington recalls a more positive reaction to the concept of a hybrid SPECT/CT and things moved amazingly fast.

However, not everyone involved in the project believed a hybrid SPECT/CT would work. "I was skeptical and thought the approach was a bit crazy," says Dr. Sandler. "And, I was totally wrong."

According to Yigal Shrem, Lead System Designer at GE Healthcare, the program's original name was Anatomical Mapping, as that was the main objective. Shrem recalls that Hermony had a chalkboard in the Haifa offices with all active programs on it, including this one. With a customer visit planned, the ELGEMS team was concerned that someone might know what they were working on because of the name on the board. So, it was quickly changed to Hawkeye, a name of a main character from the hit 1970 movie, M.A.S.H.

"ELGEMS chose some interesting names for the project: Einstein was the name for the workstation and Hawkeye was the imaging technology," Dr. Patton recalls. "They wanted to come up with a new name but I said Hawkeye just fit. It would be tough to change it to something else."

While Hawkeye was originally referred to as "inherent registration," technology, it was any but that, recalls Eitan Shaham, Global Product Marketing Manager (retired), GE Healthcare. In the early years, SPECT/CT required much realignment to ensure accurate image fusion. Landmark-based image software registration would also not work due to the lack of landmarks in the SPECT imaging data, he explains.

#### The beginning of hybrid imaging

From the 1997 meetings in Haifa and Glasgow, Hawkeye product development at ELGEMS moved swiftly. In fact, a common perception from all involved clinical partners—Drs. Turkington, Sandler, Patton and Israel—was how fast the ELGEMS engineering team took an idea and developed a product.

A key challenge was the selection of a CT system that could provide localization and attenuation correction at a very low mA and, hence, very low dose. According to Hermony, the ELGEMS development team created a concept for such a low dose CT that would be significantly lower in cost than a typical diagnostic CT but could also be attached to a nuclear gamma camera gantry. The goal was to deliver financial and economic value to potential customers with a system that would cost only one-third more than a conventional gamma camera.

"While today we can see the justification for a diagnosticquality CT for quantification, at that time our priority was to minimize cost to deliver a lower total cost of ownership," Hermony says. "And, we wanted clinicians to have the ability to obtain a hybrid anatomical and functional image with the dose of just one, not two, systems."

One valuable lesson learned with the early systems was that the table sag for a heavy patient was different for SPECT and

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Figure 4. One of the first product photos of Hawkeye.

CT (because of the different amount of table extension for the two), resulting in mismatched images. So, ELGEMS put rollers in the gantry to catch the table and prevent the sag. Commercial PET/CT systems, which came later, all needed a similar way to address the problem.

"It was just an incredible environment where a few of us from academia were invited to come to Haifa for a couple days and provide feedback on the development," says Dr. Turkington. "Just the fact the company was having these meetings in a fairly intimate environment was a wonderful thing to be a part of. Hawkeye is a great example of academia and industry working together."

Dr. Patton credits the academia-industry collaboration as a key factor that changed the way manufacturers developed new medical systems—with extensive clinical input. "This was unheard of at that time, to take a group of physicists and clinicians and sit them down with engineers at a manufacturer to discuss what needed to be done and how to go about doing it."

Professor Israel recalls that while there was much excitement, there was also a good dose of skepticism. "We had to convince the developers that they had a breakthrough technology. Not everyone was so convinced this would work."

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That all changed once the first images were acquired on Hawkeye.

"I was flabbergasted from the first moment," Professor Israel adds. "At the moment we saw the first images, there was an understanding of the power of this new modality. Then, the big challenge we had was to provide the evidence-based data that could be published to show what this new modality could really do.

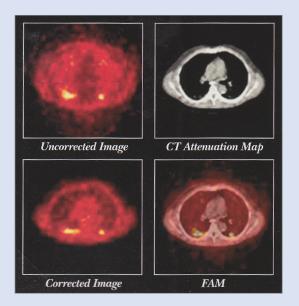


Figure 5. Highly accurate attenuation maps from the CT scan help create high-quality functional anatomic mapping images.

"I had a feeling that this would move our field from guessing to knowing, but we needed a large number of patient cases to prove our hypothesis," she says.

In early 1999, the first Hawkeye was delivered to Vanderbilt University. Dr. Sandler recalls that GE executives were on hand to witness the very first scans on a patient with melanoma. The SPECT scan depicted increased uptake in a tumor that correlated perfectly with the CT. They were also able to discern the heart and liver in the SPECT/CT. However, the team noticed something else they didn't expect or know at the time; additional lesions indicating metastatic melanoma that changed the patient's treatment plan.

As a nuclear medicine physician, Dr. Sandler was accustomed to interpreting gamma camera and SPECT images. However, once he saw the clinical impact of SPECT/CT, he began to



Figure 6. An installed Millenium VG Hawkeye.

better understand the true value of combined functional and anatomic imaging, how it enhanced specificity and how it would change the field of nuclear medicine.

"We could be more specific about what we were looking at, whether it was metastatic bone disease or a benign lesion," Dr. Sandler explains. "The ability to do SPECT/CT increased the specificity component that is at the heart of this modality."

Dr. Patton was also amazed at the very first images. He could see the future potential of a SPECT/CT that could provide attenuation correction as well as anatomical imaging.

"Hawkeye would solve the questions that plagued nuclear medicine since the 1960s: how to get anatomy in nuclear medicine," Dr. Patton says. "It was so difficult for us to keep quiet about this technology."

Subsequent beta systems were then delivered to both Duke and Rambam.

#### **Unveiling Hawkeye**

Finally, at the SNM 1999 GE user group meeting, Dr. Patton was able to share the initial work on Hawkeye that he and Dr. Sandler had done. He recalls having a captivated audience that attentively listened to the first presentation demonstrating the clinical value of a functional-anatomical imaging system.

And, there was Hawkeye in GE's booth at SNM 1999-the worldwide introduction of the very first SPECT/CT hybrid imaging system. To the backdrop of Prince's hit song, 1999, Hawkeye was unveiled to leading nuclear medicine physicians and industry. It was heralded as form meeting function. At that time, AuntMinnie.com's Editor-in-Chief Brian Casey called the development of hybrid imaging systems that combine nuclear medicine cameras with anatomic imaging modalities "one of the hottest trends in nuclear medicine."

Hawkeye combined a Millennium VG camera with an X-ray tube and digital detector that rotated around the patient while the nuclear medicine study was conducted, collecting both functional and anatomic data. After fusing the data, physicians could view the functional and anatomical data as one image. To say it was groundbreaking to the physicians and scientists at SNM 1999 is not an understatement.

GE offered the solution on new systems and also as an upgrade on installed Millennium VG cameras. The company promised it would deliver powerful information that clinicians could use to change patient management.

"Hawkeye enabled us to do a lot of things we couldn't do before," says Dr. Patton. "At the time, I said it was a total waste of money to put a diagnostic CT on a PET or SPECT. Of course, now no PET is sold without diagnostic CT. And, the majority of SPECT/CT systems have a diagnostic CT component."

Dr. Sandler agrees, noting that over time the inclusion of diagnostic CT has delivered higher resolution imaging, providing clinicians with the information they need to make a more confident diagnosis.

"The concept of fusing two images is now standard and we'll continue to see other examples in the future," Dr. Sandler adds. "Hawkeye clearly set the foundation for a technological change and a change in the way we think about and utilize hybrid imaging."

Dr. Sandler also believes SPECT/CT has propelled the relevance and sophistication of nuclear medicine.

"Clearly, the Hawkeye was the most innovative nuclear medicine system of its time," Dr. Sandler explains. "Now, SPECT/CT has become standard practice. Instead of reporting that we see something, we can say specifically what it is. The development of hybrid SPECT/CT increased our ability to answer the questions from our clinical colleagues."

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Aharon Peretz, Nuclear Medicine Research & Advanced Applications Manager (retired), GE Healthcare, believes the development of Hawkeye did more than change the field of nuclear medicine. "It started all hybrid modalities, including PET/CT and PET/MR, and propelled the future of PET imaging, how it works and where it is used."

In fact, the development of Hawkeye led directly to the creation of the Discovery<sup>™</sup>LS PET/CT system, which was launched in early 2001.

Dr. Turkington believes that the number of gamma cameras with a CT component will continue to increase, yet he believes the question of what type of CT will continue. He adds that there will continue to be pressures to have CT image quality matching that from the latest stand-alone CT systems, but there will also be pressures to keep costs down and to see the SPECT/CT needs as unique from CT alone.

"SPECT applications are evolving, so how CT is used with SPECT will also continue to evolve," says Dr. Turkington. "One driver will be the referring physicians, who will increasingly come to expect nuclear medicine studies fused with CT. Also, the demand for SPECT images to be quantitatively useful will continue to increase; maybe all SPECT systems will have a CT in the future."

Acknowledging that opinions vary, Dr. Turkington does believe that the clinical demand for quantification in SPECT imaging is growing.

Although today's SPECT/CT systems are advanced, the idea originates with Hawkeye. Professor Israel explains, "What we have today in terms of technology could only be based on what we had then. There has been a continual improvement to fulfill clinical needs, increase efficiency and address protocol limitations. It is hard to think about anything in nuclear medicine today where SPECT/CT has not made an impact. Most important is that there are two components. For too long, technological developments have focused mainly on CT. We are now facing a second revolution in SPECT technology and that will definitely lead to more significant change."

1. Jones EF, Gould RG, VanBrocklin HF. Bruce H. Hasegawa, PhD, 1951-2008. J Nucl Med, 2008;49(9):37N-38N