
Hologic Bone Densitometry and the Evolution of DXA

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Hologic is challenging the boundaries of science to advance women's bone health

Hologic officially opened its doors in 1986 and just a year later, introduced the industry's first dual-energy X-ray absorptiometry (DXA) system – today's gold standard of bone mineral densitometry – and one of many products developed by Hologic that hold the enviable number one market position worldwide. Hologic is on a mission: To help women around the world lead longer, healthier lives. It is the sole purpose for every breakthrough Hologic pursues every technology Hologic creates, every investment Hologic makes. This single-minded dedication has made Hologic a world leader in women's health, with a long track record of "firsts" in areas from cervical cancer screening to breast cancer diagnosis and osteoporosis assessment. In fact, it is in the area of osteoporosis assessment where Hologic first made its mark. In 1985, Hologic co-founders David Ellenbogen and Jay Stein began a journey that would – over the course of nearly three decades – transform the world of medical imaging

Developing the technology: From simple X-rays to the dawn of DXA

In the early years of bone mineral density (BMD) measurement, the only way to estimate bone mass was to take an X-ray of the skeleton. However, conventional X-rays were insensitive and if there were issues with bone density, they weren't apparent until approximately 30 percent to 40 percent of bone had been lost. By that time, the patient may have already suffered fractures, making it too late for therapeutic intervention. Researchers began looking for alternative methods to measure BMD – the first of which was single-photon absorptiometry (SPA). As an extension to SPA, dual-photon absorptiometry (DPA) was developed and this technology allowed for critical measurements of the spine and femur which quickly propelled DPA as the clinical choice for BMD evaluation. Both SPA and DPA utilized radioactive

isotopes as their energy source relative to evaluating bone mineral density. Hologic's Dr. Stein and his colleagues began the arduous work of bringing dual-energy X-ray absorptiometry (DXA) to reality. By using a dual-energy X-ray source Dr. Stein eliminated problems associated with decaying isotopes. As Dr. Stein discovered, DXA reduced scan times, delivered higher spatial resolution, allowed for the same measurements that were achieved with DPA, precision was within 1 to 2 percent, and dose was minimal to both patient and operator. In 1987 Hologic introduced the first bone densitometer with its proprietary DXA, Quantitative Digital Radiography (QDR™). The new Hologic QDR-1000 system would set performance standards for many years to follow. For the first time, physicians had a way to accurately and cost effectively assess bone mineral content in the spine and hip – the most vital anatomical sites for fracture risk evaluation.

Diagnosing and monitoring the treatment of osteoporosis demands accurate and precise BMD measurements. Accuracy reflects the ability to measure true value – the measurement used to determine if a patient is normal, low bone mass or osteoporosis. Precision reflects the ability to measure the reproducible value – important because measurements performed at different times may be used to monitor the impact of aging, disease or treatment of the patient. Hologic developed its Internal Reference System and Anthropomorphic QC Spine Phantom specifically to achieve maximum accuracy and precision. Since the introduction of the QDR-1000, all Hologic DXA systems have been equipped with both of these critical features:

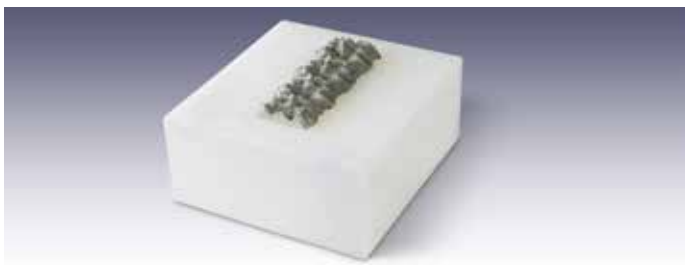
- The X-ray source of the DXA system generates alternating high and low energy pulses in a thin beam that passes through Hologic's patented Automatic Internal Reference System. By constantly comparing the patient's bone to a known value contained in the internal reference standard, Hologic systems automatically calibrate each data pixel on every scan.

- Anthropomorphic QC Spine Phantom: Hologic's Anthropomorphic QC Spine Phantom confirms system stability with a life-like standard that simulates in vivo conditions and has exceptional sensitivity for detecting data drift. The system automatically scans the spine phantom to confirm system stability and performance.

These Hologic milestones ensure precise and consistent BMD results test after test, year after year, outperforming any other system on the market.¹ The exceptional stability and precision of Hologic QDR™ systems have made them the choice for most major government and pharmaceutical studies.



The Hologic patented calibration system provides continuous calibration.



The anthropomorphic phantom has been developed from human data.

Hologic's proven superiority

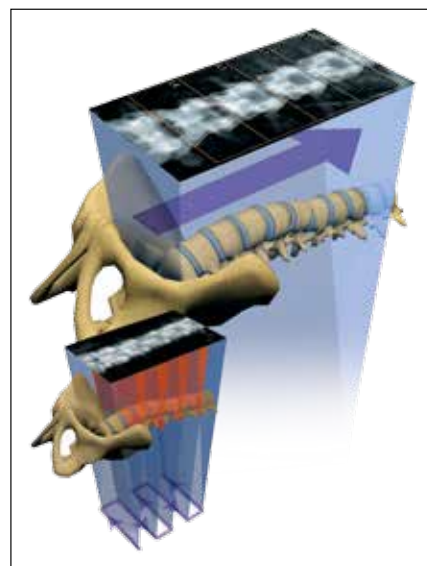
The Hangartner study measured the BMIL phantom on two GE/Lunar Prodigy and two Hologic Discovery™ scanners over a three-year period. The four units were investigated over the same time interval on the same phantom. The GE Prodigy systems continued to pass their daily quality assurance tests throughout the four year period as did the Hologic systems; although the critical point for GE Prodigy owners was that they were unaware their systems were drifting, and producing changes of more than twice the nominal precision for AP spine exams, while Hologic Discovery systems maintained precision and accuracy throughout the evaluation. This data clearly demonstrates that the GE Prodigy's daily calibration and quality assurance routines are inadequate. The precision of Hologic's DXA is 5-10 times better than GE's DXA, in turn designating Hologic the superior choice for osteoporosis evaluation.¹

Hologic: First to market with true linear fan-beam X-ray technology

From the conception of DXA, Dr. Stein envisioned the use of a fan-beam X-ray source with a multi-element detector array, which he recognized would further decrease scan time and improve efficiency. However, due to the limits of available technologies, he and his colleagues introduced the first-generation QDR system using a rectilinear scanning pencil beam. Over the following few years, Hologic scientists worked diligently to develop the world's first fan-beam DXA system – the QDR 2000. In 1991, the QDR 2000 system with Hologic's proprietary OnePass™ fan-beam technology came to market.

In 2000, Hologic pioneered the integration of BMD measurement with Instant Vertebral Assessment™ (IVA™) imaging tool, allowing point-of-care assessment of the two most definitive factors associated with osteoporotic fracture risk: low bone mineral density and the presence of vertebral fracture. Vertebral fractures are associated with increased disability and morbidity:

- Women with vertebral fractures have been shown to have a five-fold increase of having subsequent fractures and a two-fold increase in the likelihood of a hip fracture.²
- One out of every five women who have an incident of vertebral fractures will suffer a subsequent fracture within the following 12 months.²



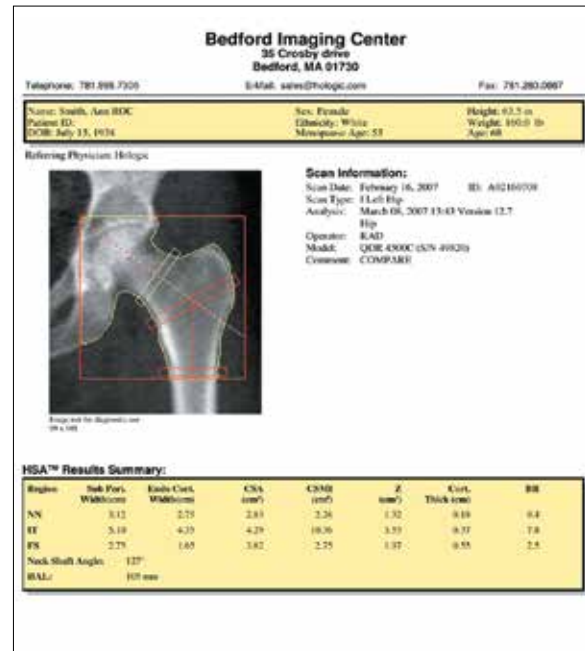
Hologic exclusive OnePass fan-beam technology.

The IVA™ imaging tool was first introduced on the Hologic's Delphi system. Delphi used a high-resolution detector array, combined with true fan-beam geometry, allowing linear scan acquisition. This design enabled rapid, high-resolution single-energy imaging, as well as superior dual-energy bone density measurements.³ IVA of the T4 to L4 vertebrae could be performed in as little as 10 seconds. The result was the highest resolution vertebral imaging, dramatically improving the detection of vertebral fractures.⁴ By combining IVA with BMD, the two strongest risk factors for future fractures could now be obtained on the same device with little additional exam time.

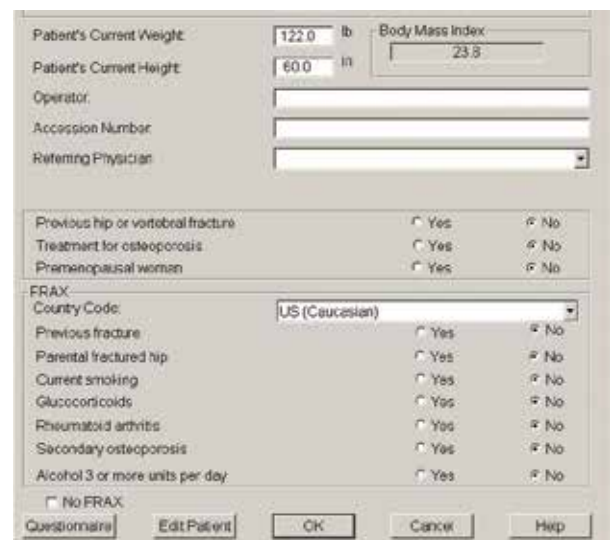
Hologic: First to integrate Hip Structure Analysis™ software and FRAX® 10-year Fracture Risk Assessment into its DXA systems

While BMD is recognized as a strong predictor of fracture risk in osteoporosis, structural effects on bones that are important in determining their mechanical strength cannot be easily determined from BMD alone. To address this, Dr. Thomas Beck, Associate Professor of Radiology in the School of Medicine at The Johns Hopkins University, applied his work with Hip Structure Analysis (HSA®) principles to calculate both BMD and the structural geometry that underlies bone strength from DXA measurements. In 2006, Hologic signed a licensing agreement with The Johns Hopkins University and the Applied Physics Laboratory to integrate the work of Dr. Beck and his colleagues on HSA into Hologic densitometers. HSA is the leading bone structure analysis for DXA scans used in research and pharmaceutical studies, with its prediction of bone strength the subject of many peer-reviewed publications.

In 2008, Hologic incorporated the World Health Organization's (WHO) Fracture Risk Assessment (FRAX) Calculator into its bone densitometer systems. WHO developed FRAX as a tool to help healthcare providers identify and proactively treat patients with a high risk of bone fractures due to low bone mass and other risk factors. While the T-score remains the standard for diagnosing osteoporosis, FRAX breaks new ground, enabling healthcare providers to identify patients with a high risk of experiencing bone fractures within a period of 10 years. By combining 11 of the highest risk factors, including age, personal history of fractures, and family history of fractures, plus country-specific life expectancy and country-specific fracture data, FRAX identifies patients who are at high risk of fracture, but would not be candidates for preventive therapy using the traditional T-score. Hologic quickly integrated the FRAX calculator into their products for improved patient care.



Exclusive Discovery™ feature enables a new dimension in bone health assessment with Hip Structure Analysis.



FRAX configuration screen

Hologic: First DXA system to provide assessment of three major health issues

The Hologic Discovery™ system was the first to employ High Definition Instant Vertebral Assessment™ (IVA™-HD) imaging tool, enabling physicians to identify spine fractures with one rapid, low-dose, single-energy image at double the resolution of previously available techniques. As a result of its superior high-definition digital DXA detectors, physicians began using Hologic Discovery systems for other applications

beyond BMD measurements, specifically to visualize calcified plaques in the abdominal aorta, which has been shown to be a significant indication of heart disease and stroke.^{5,6}

While DXA has long been considered the gold standard in the precise measurement of a person's percent body fat, there was a lack of accurate reference data from which to define healthful levels of percent body fat and muscle mass. The U.S. Centers for Disease Control's "National Health and Nutrition Examination Survey" (NHANES) took on the task of collecting accurate body composition data and in 2008 released the NHANES survey data. In 2011, Hologic was the first DXA systems manufacturer to incorporate NHANES data into its systems. With the introduction of the Hologic Advanced Body Composition™ assessment with InnerCore™ visceral adipose tissue assessment into its Discovery system,

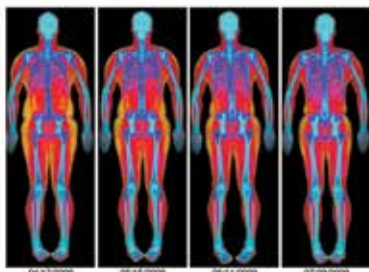
Hologic IVA-HD linear single energy vertebral fracture assessment.



Calcifications in the abdominal aorta.



Color tissue mapping displaying patient's progress.



Hologic gave physicians a quick, accurate and precise low-dose X-ray exam to help assess subcutaneous and visceral fat, lean tissue and bone. Some of the diseases and conditions for which body composition and visceral fat assessment values are useful include chronic renal failure, anorexia nervosa, obesity, AIDS/HIV, cystic fibrosis and potential risk of cardiovascular disease. With these additional applications, the Discovery system is now the only DXA system to provide a single comprehensive platform for the assessment of osteoporosis including vertebral fracture assessment, along with cardiovascular disease and obesity.

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