# *Osteoscanner MOsteoDD*

## *Multi-electrode*

## *Osteoporosis*

## *Detection Device*

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This confidential Information Memorandum contains information relating to the commercialisation of the Multi-electrode Osteoporosis Detection Device ("the Proposal"). It has been prepared by the Directors of the Company, in connection with the funding of the Proposal and is being furnished to a select number of parties who have expressed an interest in funding the Proposal.

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BONE VITAE will arrange all contacts for appropriate due diligence by potential funders. All enquiries or requests for additional information should be submitted or directed to Mr Marcin Just of BONE VITAE.

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# Contents

# 1. Executive Summary

## 1.1. Overview

Osteoporosis is one of the major problems facing women and older people of both sexes globally**.** In the USA, approximately 1.5 million fractures annually are attributable to osteoporosis. In Europe, the annual direct medical costs of fractures attributed to osteoporosis run at €36bn and are expected to grow to €76.9bn in 2050.[1]

Bone Vitae S.A. (BV) have developed a patented low-cost osteoscanner (MOsteoDD – Multi-electrode Osteoporosis Detection Device) which is accurate and can be used frequently and widely to detect the early signs of osteoporosis, enabling early treatment and life style adjustment to reduce a significant burden on healthcare providers globally.

## 1.2. The Company

The company, Bone Vitae S.A., was created in Warsaw, Poland in January 2011. The company was established to develop multi-electrode measurement technology and to commercialize the created osteoscanner – MOsteoDD.

## 1.3. The Product

The MOsteoDD osteoscanner is very light, easy to use and does not use ionizing radiation because it is based upon a technique known as bio-impedance. The average measurement time is approximately only 30 seconds. The device has been designed and manufactured to recommend medical standards defined in the IEC60601 regulation. Electrical safety and electromagnetic compatibility (EMC) of the device have been tested in an accredited laboratory according to the PR EN 60601-2-10 standard. The recent developed device is already the second version. As compared to the first version, its ease of use and reliability has been improved. The product is designed especially for point of care (POC) medical screening. However, other applications are anticipated as described below.

## 1.4. Intellectual Property

Bone Vitae S.A. is the sole owner of all patent rights in Polish patent number PL 218085 and international patent application number WO 2011/102743 A1 for the methodology and device created by the scientific team and number WO 2013/128243 A1 (filed in February 2012) for the device structure, circuit and functions. Bone Vitae SA have instructed Reddie & Grose LLP, England (UK) to act as its Patent and/or Trade Mark Attorneys**.**

## 1.5. Clinical trials

The effectiveness of the method was confirmed in two clinical studies upon 79 chosen patients – postmenopausal women without fractures and chronic diseases. The statistical analysis results for the second version of the device presented here have shown that it is possible to obtain both a sensitivity and specificity above 80% against DXA.

## 1.6. Senior Management

The shareholders gained a list of superb experts in the medical and VC markets who actively participate in BV, both as members of the board, or as experts and advisors:

- **Marcin Just** – CEO and Senior Engineer R&D – Marcin Just is a scientist dedicated to physics and bio-physics. He is a co-owner of five active patents and many patent applications.
- **Professor Przemysław Łoś** – R&D Manager and President of Supervisory Board – Professor of Chemistry at the Industrial Chemistry Research Institute in Warsaw, with wide experience in bio-impedance and biomedical research, development and commercialization gathered both during domestic and international employments, including his work at Dundee and St Andrews Universities, Scotland, Spain, USA, Canada and France.
- **Michał H. Tyc** – Senior Engineer R&D – Michał Tyc holds a PhD degree in physics. Together with Mr Just, he is focussed on physics and bio-physics research.

**Marcin Just, Przemysław Łoś**, **Michał H. Tyc** are founders and inventors of the device and technology.

[1] Assessment of Osteoporosis at the primary health care level, Report of WHO Scientific Group, 2007.

# 2. Osteoporosis

The bones in our skeleton are made of a thick outer shell with a strong inner honeycomb mesh of tiny struts of bone. In osteoporosis, some of these struts become thin, making the bone more fragile and prone to break after a minor bump or fall. Breaks in osteoporotic bones are often referred to as fragility fractures. Although fractures can occur in different parts of the body, the wrist, hip and spine are the most commonly affected sites.

Having osteoporosis does not automatically mean that your bones will break; it just means that you have a *greater risk of fracture*. Thin, fragile bones in themselves are not painful but once broken pain is common and a variety of other undesirable complications can occur. Bones that break because of osteoporosis will still heal in the same way as they do in people who do not have osteoporosis, which is usually about six to eight weeks. [2][2]

## 2.1. Osteoporosis – a global problem

Osteoporosis is a global problem. The burden of osteoporosis is not only a social one but also an economic burden. In addition to its effects upon temporary or permanent loss of manpower, the treatment of osteoporosis and resultant osteoporotic fractures costs billions of euros each year. Moreover, it has been anticipated that the problem will steadily increase with increased longevity for both women and the men especially in Western European and North American countries. According to the World Population Prospects prepared by United Nations Organization[1], the ageing process will be most pronounced in the highly developed countries[2], where it is estimated that by 2040, people aged 50 years and over will constitute 44.31% of the population, and people aged 65 years or over will constitute 24% of the population signifying an increase of 10% compared with 2010.

| Region | Year | Population size (in hundreds of thousands) | | | % of people aged 50+ | % of people aged 65+ |
|---|---|---|---|---|---|---|
| | | 50+ | 65+ | Total | | |
| World | 2010 | 1 416 674 | 523 478 | 6 908 688 | 20.51% | 7.58% |
| | 2020 | 1 849 413 | 713 855 | 7 674 833 | 24.10% | 9.30% |
| | 2030 | 2 283 340 | 969 439 | 8 308 895 | 27.48% | 11.67% |
| | 2040 | 2 741 560 | 1 251 775 | 8 801 196 | 31.15% | 14.22% |
| Highly developed countries | 2010 | 436 897 | 197 303 | 1 237 228 | 35.31% | 15.95% |
| | 2020 | 495 628 | 241 727 | 1 268 343 | 39.08% | 19.06% |
| | 2030 | 538 090 | 288 365 | 1 281 628 | 41.98% | 22.50% |
| | 2040 | 568 205 | 317 518 | 1 282 277 | 44.31% | 24.76% |

The increasing percentage of women over 65 years of age and men over 70 years of age signifies a very high increase in the population at risk from osteoporosis, and requiring regular diagnostic examinations.

| Region | Sex/age | Year | Population size (in hundreds of thousands) | Population growth (year – 1 = base year) |
|---|---|---|---|---|
| World | Women 65+ | 2010 | 292 229 | - |
| | | 2020 | 394 817 | 35.11% |
| | | 2030 | 534 920 | 35.49% |
| | | 2040 | 690 171 | 29.02% |
| | Men 70+ | 2010 | 147 902 | - |
| | | 2020 | 193 393 | 30.76% |
| | | 2030 | 275 599 | 42.51% |
| | | 2040 | 372 770 | 35.26% |
| Highly developed countries | Women 65+ | 2010 | 116 539 | - |
| | | 2020 | 139 788 | 19.95% |
| | | 2030 | 165 133 | 18.13% |
| | | 2040 | 180 772 | 9.47% |
| | Men 70+ | 2010 | 55 520 | - |
| | | 2020 | 68 541 | 23.45% |
| | | 2030 | 86 133 | 25.67% |
| | | 2040 | 99 717 | 15.77% |

[2] National Osteoporosis Society.

*Source: Assessment of osteoporosis at the primary healthcare level. Technical Report. WHO Centre for Metabolic Bone Diseases, University of Sheffield, UK 2007, p. 38.*

Aside from its personal and human cost, osteoporosis is a major public health problem, with enormous social and economic impact. Worldwide it is estimated that one in three women and one in five men over the age of 50 will sustain an osteoporotic fracture. In the European Union, someone sustains an osteoporotic fracture every 30 seconds and with an ever ageing population, the annual number of hip fractures alone in the EU is expected to more than double over the next 50 years. In the year 2000 in Europe, patients sustained an estimated 3.79 million osteoporotic fractures, of which 0.89 million were hip fractures (711,000 in women and 179,000 in men). The combined risk of fractures requiring clinical attention is around 40%, equivalent to the risk for cardiovascular disease. This report captures only the annual number of hip fractures among European Union member states, rather than whole of Europe, and suggests an incidence that continues to increase. It is easier to collect data for hip fractures compared with other osteoporotic fractures, because they require hospitalisation and are thus captured in hospital admission and discharge data records. From this data we know that only half of the hip fracture patients who survive will walk again, but often not to the same degree as before the fracture.

Although osteoporosis can be reliably diagnosed and treated, studies have shown that it remains seriously under-diagnosed and under-treated. It is estimated that only one out of every three vertebral fractures requires clinical attention. Despite this, it is known that having one vertebral fracture increases the risk for sustaining additional vertebral fractures increases by five-fold within the next year, a phenomenon commonly known as the *fracture cascade*. Even in patients who present with a clinically evident fracture, appropriate diagnostic testing and subsequent osteoporosis treatment are provided in only about 20% of cases. In Europe, osteoporotic fractures account for more patient disability and mortality, than do all common cancers with the exception of lung cancer. The global burden of a disease is often measured in DALYs, or Disability Adjusted Life Years. 1 DALY equals one lost year of healthy life. Furthermore, in women over 45 years of age, osteoporosis accounts for more days spent in hospital compared with many other diseases, including diabetes, myocardial infarction and breast cancer, and is one of the most common causes of patients becoming bedridden.

Despite these alarming statistics, many countries continue to place osteoporosis low on the list of priorities in their healthcare systems presumably because osteoporosis may not be perceived to have the mortality and morbidity of other chronic diseases. However, it is clear that the burden is in fact comparable to or greater than many of the common chronic disease processes.

Since osteoporosis can result for a number of reasons and is essentially asymptomatic until a fracture occurs, there is a need to monitor high risk individuals on a regular basis so that they can be offered timely treatment.

## 2.2. Market Need

Currently, the known techniques that are used for analysing the structure and chemical composition of bones depend on performing an X-ray scan of specific sites of the skeleton that are prone to the development of osteoporosis or by analysing ultrasound echo scan images of specific bones. The techniques that use X-ray (DEXA or DXA) have very good diagnostic specificity and sensitivity; with a 95% confidence level in the case of dual energy X-ray densitometry. However, these X-ray methods are time-consuming and inconvenient. They also involve exposing a patient to the known potentially harmful effect of X-rays, and require using expensive and sizeable equipment. By comparison, ultrasound methods do not provide the same diagnostic capability, as they provide information about the mechanical properties of bones which does not reflect their structure and chemical composition accurately.

In 2007, there were just 180 DEXA scanners in the UK, the 4$^{th}$ lowest of all of the European countries in terms of scanners per 1M population. Yet the UK incidence of hip fractures increased from 11.6 per 10,000 population in 2001 to 16.4 in 2007.

## 2.3. The need for screening

It is estimated that the number of individuals at high risk of developing osteoporosis within Europe is 70 million and that it is recommended that these individuals should be screened on average 1–2 times per year. This indicates a requirement for between 70 and 140 million examinations annually within Europe. This is of particular importance since effective treatment (pharmacological and physical methods) exists to treat osteoporosis provided it is initiated in a timely fashion.

It should also be emphasized that even within the member states comprising the European Union, that the number of DXA scanners is insufficient for the number of scans that would be required annually to provide a truly preventive screening programme. (See Appendix 4). The situation is mirrored in other wealthy regions of the world. This problem is exacerbated yet further through the recent withdrawal of portable pDXA scanners from the market based upon the significant difference between forearm measurements made using whole body DXA systems (Hologic, Lunar, Norland) and the measurements made using the peripheral devices that can only measure forearm bone quality (DTX-Osteometer Hologic, PIXI-Lunar, Norland).[3]

Given the scale of the clinical problem and the need to obtain readily available and affordable methods for screening patients at risk of developing osteoporosis, it is easy to envisage why the Bone Vitae system, that has a diagnostic sensitivity and specificity similar to whole body DEXA systems, would be an attractive addition to General Practitioners and patients alike, especially when one considers its overall safety and suitability for repeated use.

## 2.4. The importance of screening tests

Screening tests are strategic examinations, which are performed on individuals or at times populations who do not have clinical symptoms of the disease process although the test can detect the disease at an early stage. The aim of screening tests is to detect the disease at a sufficiently early stage to facilitate optimal therapeutic intervention thereby reducing both the morbidity and on occasions the mortality associated with the disease process. Currently, according to the guidelines issued by the National Osteoporosis Foundation, bone mineral density should be examined in the following at risk groups of people:

- Age: 65 years and over for women and 70 years and over for men,
- All people who have experienced an osteoporotic fracture,
- People whose parents sustained an osteoporotic proximal femoral fracture at a young age; 50 years of age in the case of the father, and soon after the menopause in the case of the mother,
- Adults suffering from a disease characterized by low bone mass or loss of bone mass,
- Adults taking drugs prescribed in the case of low bone mass or loss of bone mass,
- Individuals who are treated with certain types of drugs that are known to induce osteoporosis, especially long-term treatment with corticosteroids (more than 7.5 mg daily of prednisone for a minimum of 3 months),
- Middle aged and elderly people who have a tendency to fall for medical reasons (e.g. visual or neurological impairment),
- Individuals undergoing treatment for osteoporosis in order to check the effectiveness of treatment,
- Individuals who are not receiving treatment but whose loss of bone mass as detected by a suitable screening method will necessitate treatment.

Regular examinations in people belonging to these high risk groups are recommended to establish the rate of bone loss and also to assess the efficacy of treatment. By doing so, treatments that are failing to achieve the desired therapeutic effects can be modified at a sufficiently early stage to permit the timely introduction of an alternative treatment thereby maintaining patient independence and quality of life while negating the costs of treating established osteoporotic fractures.

## 2.5. Market Size

It is generally believed that the US market and European markets are approximately the same size. Osteoporosis affects 55% of Americans aged 50 and above. Of these, approximately 80% are women. It is estimated that 1 in 3 women and 1 in 12 men over the age of 50 worldwide have osteoporosis, which is responsible for millions of fractures annually, mostly involving the lumbar vertebrae, hip, and wrist. Fragility fractures of the ribs are also common in men.

The lifetime risk of fractures of the spine, hip, and distal radius is 40% for Caucasian women and 13% for Caucasian men from 50 years of age onwards. Following a hip fracture, there is 10%–20% mortality over the subsequent 6 months. In addition, 50% of hip fractures patients will be unable to walk without assistance, and 25% will require long-term domiciliary care. The annual cost of osteoporosis to the US healthcare system is at least $5–$10 billion with a similar incidence and cost implications in other developed countries. These already high costs will increase further with continued aging of the population. In addition, the population explosion in underdeveloped countries will change the demography of osteoporosis throughout the world; the incidence of hip fracture and, presumably, other

[3] *The view of Polskie Towarzystwo Osteoartrologii i Wielodyscyplinarnego Forum Osteoporotycznego (Polish Society of Osteoarthrology and Multi-Disciplinary Forum of Osteoporosis) on diagnostic standards and osteoporosis treatment in Poland* (version of the 21st December 2005) – http://www.kcm.pl/_files/File/PDF/2006_Czerwinski_MpD_Standardy.pdf.

osteoporotic fractures will increase four-fold worldwide during the next 50 years and the attendant costs will threaten the viability of the healthcare systems of many countries. Unless decisive steps to prevent or slow the progression of osteoporosis are undertaken in the near future, a catastrophic global epidemic of osteoporotic complications seems inevitable.[4]

Direct medical costs for osteoporotic fractures in Europe are estimated at more than €36 billion annually and are expected to grow to €76.9 billion in 2050. The huge costs associated with hip fractures include hospitalisation and the after care costs of rehabilitating patients. Duration of hospital stay varies from 3 days to many weeks or even months, with the average stay being 10 days. The number of days devoted to rehabilitating patients ranges from 10 to 48 days, with an average of 20 days.

Using the UK as an example, the incidence of osteoporosis is estimated to be 14.43 per 10,000 of population (based on 2003 data), therefore putting over 9m patients at risk of sustaining an osteoporotic fracture. When one considers that the average costs associated with treating a hip fractured patient in the acute hospital setting are over £18,500 (based on 2005 figures), it is easy to envisage the enormity of the economic burden that osteoporosis places upon the UK economy.[5]

# 3. The Technology

## 3.1. Bio-impedance

The method for analysing bone structure (described in detail in the British Patent GB2449226) relates to bio-impedance spectroscopic measurements using an apparatus equipped with measuring electrodes was originally invented in 2007 by Przemysław Łoś and Marcin Just (who are both currently employed by Bone Vitae S.A.). The method consists in generating, with a use of a generator, at least one standard signal of a defined waveform, which is then applied to the bone tissue through the surrounding tissues, skin and muscles and subsequently the electrical response is generated, being an electrical potential difference caused by current flowing through the analysed tissues, and is directed to the measuring system using the same electrodes. The data related to the bone tissue structure are generated in the system.

In a biomedical engineering, bio-impedance is the response of a living organism to an externally applied electric current. It is a measure of the opposition to the flow of that electric current through the tissues, the opposite of electrical conductivity. The measurement of the bio-impedance (or bioelectrical impedance) of the humans and animals has proved useful as a non-invasive method for measuring such things as blood flow (often referred to as bio-impedance plethysmography) and body composition (known as bioelectrical impedance analysis or simply BIA).

In bio-impedance plethysmography, the measure is sometimes based on pulsatile blood volume changes in the aorta. Bio-impedance is relevant to the development of devices to measure cardiac output and circulating blood volume. Electrical conductivity can vary as a result of breathing. Because of this and other sources of variability, the reliability of bio-impedance for obtaining accurate data has been called into question. Nevertheless, the technique is used in both routine clinical medicine and research.

A method in accordance with the present invention of Przemysław Łoś, Marcin Just and Michał Tyc comprises a system of at least four electrodes (in practice 5–8 electrodes are used, 5–6 in the current *in vivo* clinical trials) placed on the skin covering the soft tissues surrounding the analysed bones, preferably a long bone. The additional screening potential field is established by **the screening electrodes** and the flow of measuring current is forced through the analysed bone by the measuring current injecting electrodes. At the same time the screening electrodes reduce the flow of the measuring current passing through the soft tissues surrounding the analysed bone almost to zero. The measuring current and potential responses as well as a phase difference between the potential response and measuring current are measured at the injecting electrodes. Next, on the basis of measured electrical parameters, the structure and chemical composition of bones are determined.

[4] The worldwide problem of osteoporosis: insights afforded by epidemiology – Riggs BL, Melton LJ 3rd. Source: Endocrine Research Unit, Mayo Clinic, Rochester, MN 55905, USA.
[5] Osteoporosis in the European Union in 2008 – published by the International Osteoporosis Foundation.

The method was originally validated by performing numerous computer simulations. This made it possible to determine the efficient configurations of all electrodes. Finally, the method was verified and the optimal electrodes configurations selected during the clinical trials.

## 3.2. Other applications

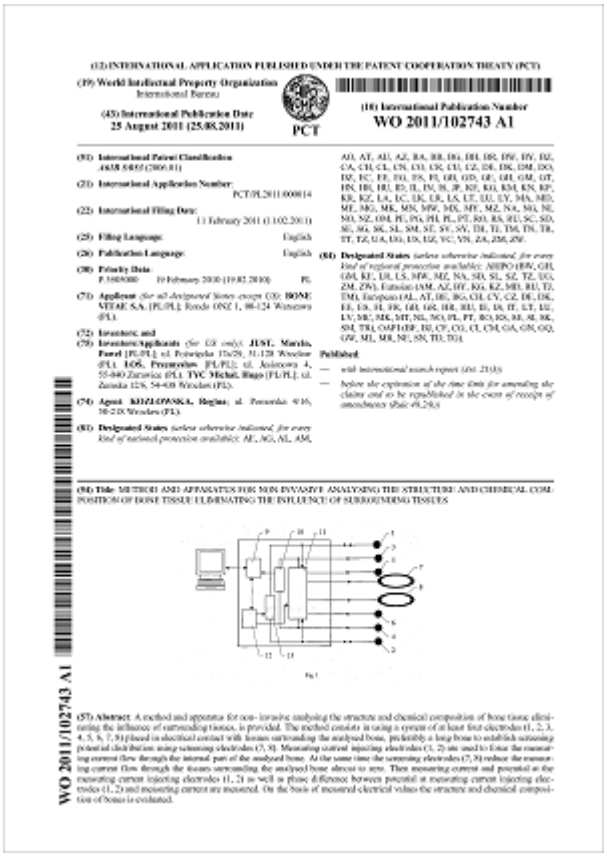
The technology might be used to detect changes in bone properties resulting from other diseases, application of medicaments and chemical substances (e.g., steroids) or environmental factors. Separate clinical studies are required for such applications.

## 3.3. IP Ownership

Bone Vitae S.A. is the sole owner of all patent rights in Polish patent number PL 218085 (granted in April 2014) and **international patent application number WO 2011/102743 A1** for the methodology and device created by the scientific team. This patent covers all rights for the method of treatment and detection of osteoporosis. The application entered the National Phase in Australia, Canada, China, Japan, South Korea and the United States as well as the European Regional Phase, which covered the European patent.

A second patent application number WO 2013/128243 A1 is called Method for Controlling Electrodes for Bio-impedance Measurements and Control Circuit for Electrodes for Bio-impedance Measurements concerning the device structure and functions.

Bone Vitae SA have instructed Reddie & Grose LLP, England (UK) to act as its Patent and/or Trade Mark Attorneys.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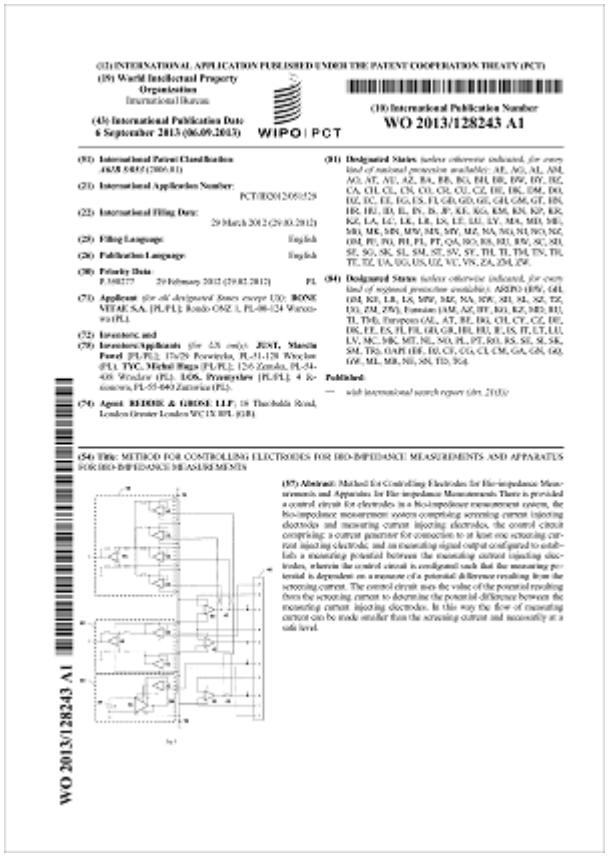
(54) Title: METHOD AND APPARATUS FOR NON-INVASIVE ANALYSING THE STRUCTURE AND CHEMICAL COMPOSITION OF BONE TISSUE ELIMINATING THE INFLUENCE OF SURROUNDING TISSUES

WO 2011/102743 A1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(54) Title: METHOD FOR CONTROLLING ELECTRODES FOR BIO-IMPEDANCE MEASUREMENTS AND APPARATUS FOR BIO-IMPEDANCE MEASUREMENTS

WO 2013/128243 A1

# 4. Product

The technology used allows you to build a small, easy to use (see image 1), battery (accumulator) powered and safe device. The device can easily be designed and manufactured to meet the requirements of medical standards defined in the IEC 60601 regulation.

The device is practically operator independent (on the assumption that electrodes are positioned correctly). This is not to suggest that the product can or should be used by anyone, simply to state that results generated, will be accurate at the levels quoted independently of the operator. Only a short training is required to properly locate the electrodes on patients forearm and it is expected that there will be substantial use of the product in the hands of the practice nursing staff where the reading would be taken before the patient sees the doctor – the nurse would simply provide the doctor with the results print out. The product also has application in domiciliary environments where the unit could easily be taken to patients who cannot make it into the practice easily.

## 4.1. Currently available device

As it was mentioned, the recently developed device is already the second version. As compared to the first version, its ease of use and reliability has been improved. Electrical safety and electromagnetic compatibility (EMC) of the device have been tested in an accredited laboratory according to the PR EN 60601-2-10 standard.

### 4.1.1. Device Performance

**Accuracy:** Sensitivity of 90% and specificity of 74% against DEXA (it can be better balanced to sensitivity and specificity > 80% simply with diagnostic maps redefinition).
**Power consumption:** 150 mW in standby, 1.5 W during measurements.
**Measurement time**: < 40 seconds.

### 4.1.2. Interfaces

- On/Off physical switch,
- Start button,
- 4 LED indicators for READY, HIGH RISK, LOW RISK and UNSURE.

### 4.1.3. Communications

None, but ready for optically separated USB.

### 4.1.4. Operation

- 4xAA accumulators, externally recharged
    - Battery Life (from fully charged, new cells) – 4 hours continuous operation (> full day's use),
- Auto switch off (time out period).

### 4.1.5. Form factor

- Structured to contain all electronics/batteries in an enclosure that is:
    - Easily portable,
    - Robust (can be put into the trunk of a car etc.).

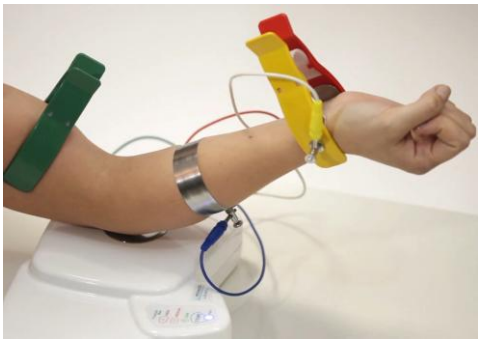


**Image 1.** The MOsteoDD second prototype used during clinical trials

## 4.2. Future devices

The final product is anticipated to meet the requirements described below.

### 4.2.1. Device Performance

**Accuracy:** Sensitivity of 95% and Specificity of 80% against DEXA.

### 4.2.2. Interfaces

- On/Off physical switch,
- 4-inch touch screen to bring in additional patient data,

### 4.2.3. Communications

- Optically separated USB,
- Bluetooth,
- Wi-Fi.

### 4.2.4. Operation

- Built-in Ni-MH or Li-Ion accumulator (recharged when supply is connected),
- Auto switch off (time out period).

### 4.2.5. Form factor

- Miniature device. Size limited by electrodes dimensions.

### 4.2.6. Additional

- Firmware upgrades. Anticipated to be web driven,
- Device registration for field upgrades.

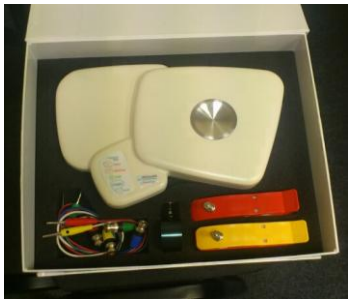



**Image 2.** Full device, full set, and package.

## 4.3. Competitive advantages of the MOsteoDD osteoscanner

The device provides accurate measurements from a compact, portable easy to use device.
Features include:

- Easy to use,
- High level of accuracy,
- Enables monitoring of patient condition,
- Operator independent,
- Safe and non-threatening,
- Portable,
- High sensitivity to pathological changes,

- Non-invasiveness – a measurement is made using electrodes applied to the body externally and the used currents have extremely low amperage,
- No ionizing radiation (no X-rays) is used which means lower degree of harm to the patient and no need for a specially equipped space for installing the device,
- Short time of the examination (measurement),
- Relatively low cost of the measuring device, its small size and low power consumption.

The MOsteoDD device is not an alternative to DEXA – it is designed to "serve on the front line" as a screening device enabling an initial selection of individuals who should be subjected to a more thorough examination. "Treatment without screening (with either semi-quantitative or qualitative methods) is economically ineffective".

Another factor that makes the proposed MOsteoDD osteoscanner attractive is its size. The device for quantitative ultrasonography QUS weights about 10 kilograms and is 70 cm long which does not make it a very convenient equipment for POC tests. Peripheral scanners are a little bit smaller but their diagnostic efficiency is questioned. Axis densitometers because of their size require a specially adapted room and cannot be transported.

Apart from diagnostic potential and the size of the group of individuals at risk of developing osteoporosis, the market/demand is determined also by the number of GPs (who are considered to be the main target) as well as by the level of health protection expenditure. The number of GPs per 100 thousand inhabitants is growing in the majority of countries. This trend combined with increasing commercialization of health services will cause rise in competition between members of this profession. The scope of available medical examinations will certainly constitute one of key factors on the health service market. Taking into account aging of the population, a lot of GPs will be interested first of all in medical devices useful in diagnosing diseases typical of individuals over 60 years of age.

Analysis shows that the number of GPs in the European Union is growing. Simultaneously, because of low birth rates, the number of patients per one physician is diminishing. The health services are more and more dependent on the market mechanisms and it should be expected that the price of medical services will drop, leading to the growth of competition between the physicians. Apart from expertise and reputation of a specialist, the most important factor excluding the price of the service is the scope of available medical examinations and the quality of the medical devices the practice is equipped with. Growing consciousness of the dangers related to osteoporosis as well as systematic osteoporosis screening campaign will certainly cause an increased interest in this type of diagnostic tests among patients.

# 5. Data Collection Studies/Clinical trials

These trials have been the most important milestone for Bone Vitae. To date the company has run two clinical tests demonstrating high level of alignment between the device and the gold standard (DEXA). The clinical trials which have been realised are sufficient to obtain CE mark for the Bone Vitae product and start its sale in 2015.

## 5.1. Independent clinical validation

A clinical *in vivo* trials have been carried out at SYNEXUS Medical Centre in Warsaw. Synexus Warsaw is a part of the world's largest multi-national company entirely focused on the recruitment and running of clinical trials at its own Dedicated Research Centres with HQ in Manchester. The director of clinical trials was Dr. Andrzej Sawicki. The permission no. KB/802/11 to carry out the clinical trial has been issued by Bioethical Commission of Regional Medical Chamber in Warsaw.


According to the protocols, the clinical trial has been carried out on 79 selected female patients, age 40+. The rejection criteria were applied such that only the healthy patients and patients with osteoporosis/osteopenia take part in the trial. Each patient underwent both full (hip, forearm and spine) DEXA examinations and bio-impedance osteoscanner examination. Bio-impedance measurements were carried out using well known 2, 4 electrodes method and a new 5–6 electrodes method. The correlation was established between bio-impedance and DEXA results (especially BMD, Z-score and T-score).

Based on the data gathered the statistics were used to build a correlation map to present the direct combination of two parameters: T-score results basing on DEXA technique [Bone Mineral Density – BMD based] measured on patients forearm and Bio-impedance measured by MOsteoDD [given in Ohms] and our patent pending SCREENING POTENTIALS METHOD described above. A very good correlation and success rate of MOsteoDD in comparison with DXA forearm T-score has been observed.

## 5.2. Accuracy – Sensitivity and Specificity

The first 41 patients were examined using the first version of the device during the first stage of clinical trials. Results from these clinical trials were used to select best electrode configuration (the easiest-to-use, reliable and sensitive enough) for next version of device. For this reason, statistical analysis carried out for the first stage has been reduced to a minimum, but even trivial analysis showed significant effectiveness for selected frequencies (see chart 1) and T-score.

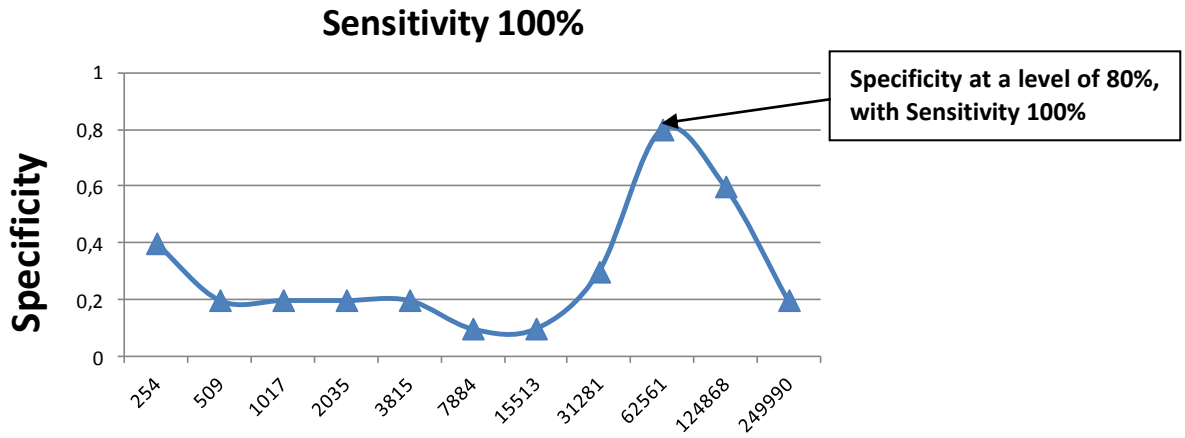



**Chart 1.** Specificity for different measurement frequencies (assuming classification set for 100% sensitivity). Sensitivity: osteopenia + osteoporosis; Specificity: Sound/Normal

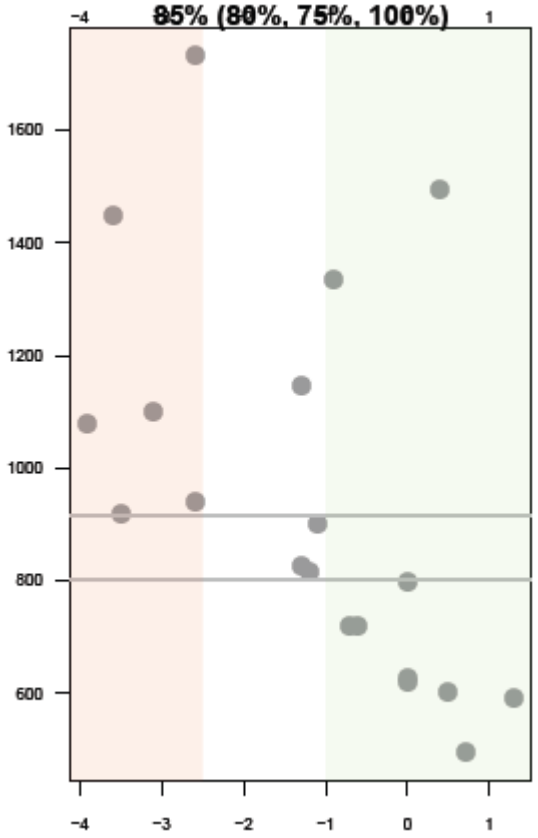



**Chart 2.** Measurement data for *Z'* at frequency 62 kHz

Chart 2 shows measurement data for one frequency. The lower horizontal line is the separation line for a two-class classification (one class is sound and the other is osteopenia + osteoporosis). For this line the overall accuracy is 90% (accuracy for osteopenia + osteoporosis is 100% and for sound 80%, because 2 points over 10 of sound patients are above horizontal line at 800 Ohms).

The best success ratio was obtained with the use of Bone Vitae “6 electrodes” method.

During the second clinical trial 38 patients were tested a new version of the device; 27 patients had complete data from two visits and the resulting data from the measurements were used to verify the effectiveness of the second version of the device.

The second version of the device has been modified to maximize the ease of use and reliability, at the expense of a slight reduction in sensitivity. The results confirmed that the desired effect has been achieved: throughout the second clinical trial were only isolated cases of failed measurements and accuracy was better than 80%. For data analysis were applied advanced statistical methods and a final model using Random Forests was proposed, using all 47 predictive variables (44 bio-impedance variables, weight, height and age).

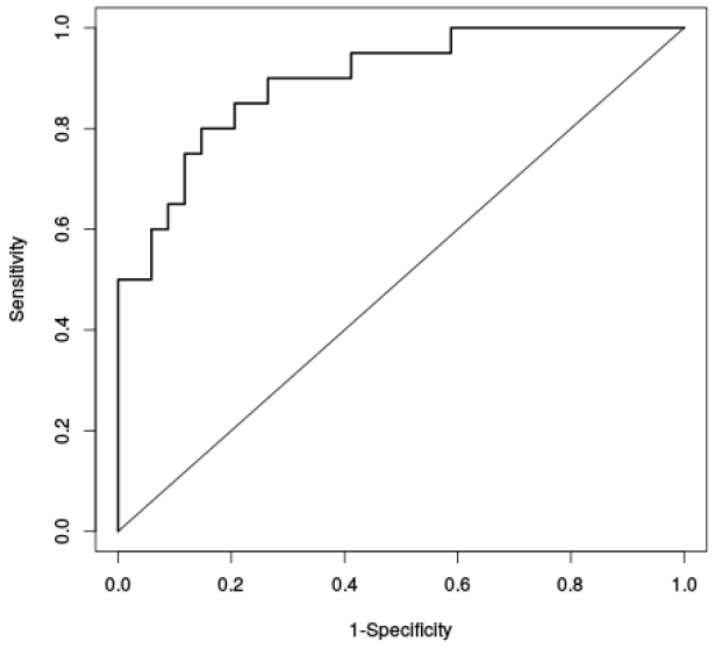



**Chart 3.** ROC curve for final discrimination model using Random Forest and limiting T-score = -2.

It can be shown that the achievable values are 90% for sensitivity at 74% specificity against DEXA.

## 5.3. Next steps

The next possible step is to undertake a multicentre validation of the device output. It is proposed that these studies would take place both in Europe and the USA. The goal of the studies is not only to prove the sensitivity and specificity expectations against the gold standard, but also to collect demographic data on a wide spectrum of patients. This will enable improvements and enhancements to both the device output and applicability.

The technology might be used to detect changes in bone properties resulting from other diseases, application of medicaments and chemical substances (e.g., steroids) or environmental factors. Additionally Separate clinical studies are required for such applications.

# 6. Quality and Regulatory Standards

## 6.1. Quality

In July 2012 Bone Vitae S.A. signed an agreement with CEMED INFO Ltd. for the services of implementation of a quality management system in accordance with the requirements of ISO 13485:2005 on the conformity assessment of medical devices. Bone Vitae will implement this system before end of 2014, and it will be applied to all outsourcing (data and product). The company will be audited by a Notified Body appropriate for the company in which it operates.

## 6.2. Standards

As a Class II active medical device the product is obliged to meet the requirements of Harmonised stand EN IEC 60601 and supplemental requirements. These will be undertaken at an established testing group (TUV Nord).

To meet the requirements for CE Mark approval the company must operate and have been audited to compliance with EN 13485 (Medical Devices) and have an established Quality System.

# 7. Sales and Marketing

## 7.1. Direct Sales

The basis for sales of the MOsteoDD is its ability to enable extremely cost effective scanning of the general population and at the same time enable sufficiently accurate measurements to allow treatment effectiveness to be monitored.

Initial sales will be made in Poland, this is a market with a strong social medicine environment, where the volume proposition of the product is readily apparent. Emphasis will be made to the regulatory and healthcare bodies demonstrating the value of screening:

- Identification of undiagnosed osteoporosis,
- Few fractures (hips, pelvis, vertebrae),
- Fewer hospital stay days:
    - Resultant reduction in healthcare costs,
- Maintenance of Quality of life for a high number of patients.

## 7.2. Licensing

First mover advantage enables the possibility of securing licensing deals with external parties additionally the company will actively explore possible purchase options – e.g., pharmaceutical companies. Trade Sale opportunities will be explored when the business case supports this.

# Appendices

## 8. Appendix 1: Potential by country

Diagnostic potential of osteoporosis in selected countries (data as of 2009 or any other available year (not earlier, however, than 2007).

| Country | Number of DXA per one million inhabitants | Average waiting time for an exam in Public Health System (in days) | Maximum waiting time for an exam (in days) | Cost of one DXA scan of a hip and spine |
|---|---|---|---|---|
| **Japan** | 82 | 0 | 0 | 44.00 € |
| 100 per cent cost coverage | | | | |
| **USA** | 35.5 | 0 | 0 | 130 € – 182 € |
| Coverage depends entirely on the rules assumed by the insurer. In Medicare case the coverage is 80% of the accepted exam price. | | | | |
| **Cyprus** | 43 | 90 | 120 | 76.00 € |
| The following economic criteria are taken into account for exam reimbursement: family size, chronic diseases, emergencies. Out of 35 available scanners, 3 belong to the Public Sector, the rest is owned by private practices. | | | | |
| **Belgium** | 38 | 1 | 3 | 40.00 € |
| Reimbursement of exam cost was restored at the beginning of 2009 and the total budget for these expenses is 2.5 million euro. It depends on certain criteria. | | | | |
| **Portugal** | 32.8 | 15 | 30 | 100 € – 150 € |
| No data | | | | |
| **Austria** | 26.7 | 10.5 | 14 | 35.00 € |
| Restricted reimbursement of costs for a certain categories of patients belonging to the higher risk group: over 65 years of age, with diseases caused by side effects ( bone mass loss) of certain types of chemotherapy, subsequent cases of fracture | | | | |
| **France** | 24 | 14 | 30 | 40 € |
| 70% exam cost reimbursement if a patient belongs to the higher risk group: irrespective of age or sex in case of a disease or if patient undergoes a treatment increasing the risk of bone mass loss; postmenopausal women with low BMI (< 19) and women who entered menopause aged 40 and earlier, children of parents with diagnosed low BMD; people who underwent a long-term therapy with certain steroids. | | | | |
| **Malta** | 20 | 180 | 180 | 75.00 € |
| The DXA exam is free on National Health service while in case of private sector the costs are sometimes reimbursed by the insurer. Public sector possesses 2 DXA scanners, 18 DXA scanners belong to private sector | | | | |
| **Slovenia** | 20 | 10 | 10 | 25 € – 50 € |
| DXA scan is still full price in case of primary osteoporosis. It is 100% refundable in case of secondary osteoporosis. There are certain discounts for Osteoporosis Society members. | | | | |
| **Greece** | 18 | 50 | 50 | 104.00 € |
| 100 per cent refund. | | | | |
| **Ireland** | 14.4 | 140 | 365 | 140.00 € |
| No exam cost refund | | | | |
| **Finland** | 14.1 | 1.5 | 3 | 100.00 € |
| Main criterion for reimbursement is a requirement of physician referral. DXA scan cost on Public Health Service is included in | | | | |

| | | | | |
|---|---|---|---|---|
| fixed charges for a visit at outpatient's clinic and charges for a stay at hospital and is not reimbursed. | | | | |
| **Slovakia** | 13.1 | 14 | 21 | 30.00 € |
| Scan cost i.e. 30 euro is reimbursed every time. | | | | |
| **Hungary** | 13 | 35 | 42 | 30.00 € |
| Patient has the right to have DXA scan reimbursed once in two years. pDXA/QUSexams were reimbursed until 2006 – starting from 2007 it is not refunded. | | | | |
| **Italy** | 11 | 87.5 | 168 | 82.00 € |
| Exam cost reimbursement is restricted to the patients who either fulfil one of so called important risk criteria or three unimportant ones (it should be stressed however that age 65 and over belongs to the second group of factors). | | | | |
| **Germany** | 10.9 | 30 | 180 | 40.00 € |
| Fully reimbursed on the condition that a patient suffered a fracture earlier. | | | | |
| **Recommended number of DXA scanners per one million inhabitants** | 10.6 | | | |
| **Sweden** | 9 | No data | 180 | 180.00 € |
| 100 per cent reimbursement with no restrictions. | | | | |
| **Spain** | 8 | 153 | 180 | 120.00 € |
| 100 per cent reimbursement with no additional restrictions. | | | | |
| **Denmark** | 7.4 | 28 | 196 | 200.00 € |
| 100 per cent reimbursement with no additional restrictions. | | | | |
| **Estonia** | 7.4 | 21 | 28 | 17.00 € |
| 100 per cent reimbursement provided a patient is referred by her/his GP or a specialist. | | | | |
| **Netherlands** | 7.2 | 24.5 | 84 | 100.00 € |
| 100 per cent reimbursement provided a patient is referred by her/his GP or a specialist. | | | | |
| **Latvia** | 5.2 | 7 | 7 | 50.00 € |
| Exams are full price and are non-refundable. | | | | |
| **Bulgaria** | 4.1 | 0 | 0 | 40 € – 75 € |
| 10 € is reimbursed for each exam on National Health Service provided that a patient belongs to one of the following groups: patients with hyperparathyroidism, patients suffering from hypogonadism, patients after organ transplantation. | | | | |
| **Lithuania** | 4.2 | 10 | No data | 15 € – 28 € |
| Exams are full price and are non-refundable. | | | | |
| **Czech Republic** | 4 | 14 | 21 | 20 € – 26 € |
| 100 per cent reimbursement for patients belonging to the higher risk of osteoporosis group | | | | |
| **Poland** | 3.9 | 60 | 90 | 9 € – 40 € |
| 100 per cent reimbursement provided a patient is referred by her/his GP or a specialist. | | | | |
| **Great Britain** | 3 | 42 | 252 | 69.00 € |
| Fully reimbursed provided a patient fulfils the criteria (in accordance with guidelines of National Institute for Clinical Excellence (*NICE*)) | | | | |
| **Romania** | 4 | 5 | 14 | 10 € – 40 € |
| 10 € is reimbursed for each exam without restrictions. | | | | |
| **Luxemburg** | 2.3 | 17.5 | 28 | 70.00 € |

| | | | | |
|---|---|---|---|---|
| 80% of exam cost is reimbursed. | | | | |
| **Armenia** | 1.3 | No data | No data | No data |
| Exams are full price and are non-refundable. | | | | |
| **Azerbaijan** | 0.9 | No data | No data | 130.00 € |
| Exams are full price and are non-refundable. | | | | |
| **Belarus** | 0.8 | 45 | No data | 20.00 € |
| Exams are full price in principle. With the exception of the situation when a patient with Belorussian citizenship receives a physician referral. | | | | |
| **Russia** | 8.6 in Moscow – 0.6 in the rest of the country | No data | No data | 12 € – 60 € |
| Exams are non-refundable. | | | | |
| **Moldova** | 0.5 | No data | No data | 30.00 € |
| Exams are non-refundable because both scanners belong to private practices. | | | | |
| **Georgia** | 0.4 | No data | No data | 90.00 € |
| Exams are non-refundable. | | | | |
| **China** | 0.35 | 2 | No data | 15 € – 77 € |
| Exams are non-refundable. | | | | |
| **Ukraine** | 0.3 | No data | No data | 13 € – 39 € |
| Exams are non-refundable. | | | | |
| **Kazakhstan** | 0.3 | No data | No data | 22.00 € |
| Exams are non-refundable. | | | | |
| **India** | 0.2 | 0 | 0 | 65 € – 78 € |
| Exams are non-refundable. | | | | |

*Source: EU Osteoporosis Report 2007-2008 (some data from 2006) – according to the information received from EU Osteoporosis Consultation Panel Members* and Eastern European & Central Asian Regional Audit (report IFO)

# 9. Appendix 2: Competitive Environment

At present the following densitometric methods are available for use in the diagnostic process[6]:

- Roentgen Absorptiometry RA,
- Single X-ray Absorptiometry SXA,
- Dual X-ray Absorptiometry DXA,
- Quantitative Computerized Tomography QCT,
- Quantitative Ultrasonography QU.

**Table 1. Characteristic of different densitometric methods.[7]**

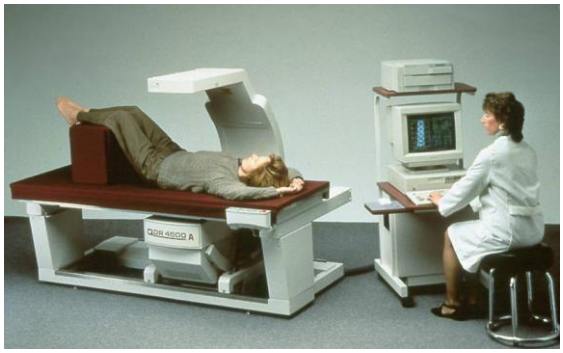
| Method | Measurement site | Repeatability error – precision (%) | | Measurement time (in minutes) | Effective dose (µSv) |
|---|---|---|---|---|---|
| **pDXA** | Forearm | 1 | 2.5 | 2 | 0.05 |
| **DXA** | spine AP | 1 | 5–6 | 5 (30s) | 0.5 (2) |
| | proximal femur | 1.5 | 5-8 | 8 (30s) | 1.4 (5.4) |
| | total body | 11 | 1–2 | 16 (7) | 4.6 (3.4) |
| **QCT** | Spine | 2–4 | 5–10 | 10 | 100 |
| **PQCT** | Forearm | 0.81 | 1–2 | 3 | 1 |
| **QUS BUA** | Heel | 1–5 | - | 2 | 0 |

Current techniques for analysing the structure and chemical composition of bones consist of performing an X-ray scan or analysing ultrasound echo scan. The techniques using X-ray (DEXA or DXA) are distinguished by a very good specificity and sensitivity at 95% level in the case of a dual energy X-ray densitometry (absorptiometry) method but they are time-consuming and troublesome/inconvenient. They also involve exposing a patient to a harmful effect of X-rays, and require using expensive and sizeable equipment. Ultrasound methods are, on the other hand, not very reliable as they are based on a measurement of mechanical properties of the bones which do not reflect the structure and chemical composition accurately.

## 9.1. DXA - currently the most popular and widely used competitor

Dual-energy X-ray absorptiometry (DXA, DEXA) it is the most popular technique to measure bone density (BMD). Two X-ray beams with different energy levels are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Dual-energy X-ray absorptiometry is the most widely used and most thoroughly studied bone density measurement technology.

DXA scans are used primarily to evaluate bone mineral density. DXA scans can also be used to measure total body composition and fat content with a high degree of accuracy comparable to hydrostatic weighing with a few important caveats. However, it has been suggested that, while accurately measuring minerals and lean soft tissue (LST), DXA may provide skewed results as a result of its method of indirectly calculating fat mass by subtracting it from the LST and/or body cell mass (BCM) that DXA actually measures.



There are some variables in addition to age that are suggested to confound the interpretation of BMD as measured by DXA. One important confounding variable is bone size. DXA has been shown to overestimate the bone mineral density of taller subjects and underestimate the bone mineral density of smaller subjects. This error is due to the way by which DXA

[6] Czerwiński E., Chrzan R.: Współczesne techniki obrazowania osteoporozy. Twój Magazyn Medyczny. Osteoporoza II, 8/2005, rok X, 8(157); 7–16
[7] http://www.kcm.pl/_files/File/PDF/2002_Dzialak_Czerwinski_Diagnostyka_OP_OTR.pdf. Data for fan beam devices are in brackets.

calculates BMD. In DXA, bone mineral content (measured as the attenuation of the X-ray by the bones being scanned) is divided by the area (also measured by the machine) of the site being scanned.

Because DXA calculates BMD using area (aBMD: areal Bone Mineral Density), it is not an accurate measurement of true bone mineral density, which is mass divided by a volume. In order to distinguish DXA BMD from volumetric bone-mineral density, researchers sometimes refer to DXA BMD as an areal bone mineral density (aBMD). The confounding effect of differences in bone size is due to the missing depth value in the calculation of bone mineral density. Despite DXA technology's problems with estimating volume, it is still a fairly accurate measure of bone mineral content.

DXA uses X-rays to assess bone mineral density. However, the radiation dose is approximately 1/10 that of a standard chest X-ray.

It is important for patients to get repeat BMD measurements done on the same machine each time, or at least a machine from the same manufacturer. Error between machines, or trying to convert measurements from one manufacturer's standard to another can introduce errors large enough to wipe out the sensitivity of the measurements.

DXA results need to be adjusted if the patient is taking defined medicines or supplements.

## 9.2. Cost per test comparison

**DEXA** **UK £ 50.0**
**MOsteoDD** **UK £ 4.70**

**(DEXA requires highly trained staff, the MOsteoDD osteoscanner is user independent.)**

Source: DXA costs estimations based on: Crisis in Osteoporosis Care in the United States, The International Society For Clinical Densitometry, 2007.

The above table compares cost per test between DEXA and MOsteoDD, it should be noted that the DEXA test is only available in larger, general hospitals, requiring a visit by the patient along with attendant waiting time and transport costs. The MOsteoDD is a portable POC device which can be used either at the local General Practitioner office, or as a home test by a district nurse, reducing the upheaval for the patient and also health care costs.

Generally medical devices are available through authorized dealers or directly from producers. Their price depending on the type and the equipment ranges from few  to few hundred thousand EUR.

In the case of diagnostic devices using dual-energy X-ray absorptiometry, it is necessary to add the cost of adapting a room where it is to be located, medical personnel salaries and spare parts cost that can reach ¼ of a device initial price. Stationary densitometers are purchased by hospitals and large health care centres. Portable devices are offered to smaller medical facilities. Advertising and promotion which is directed to specialists concentrates on device parameters and emphasizes high degree of technological advancement as well as additional options such as possibility of transmitting the results via the Internet.

Based on the above, we do not consider DXA as a competitor. We believe DXA and the MOsteoDD osteoscanner are complementary solutions, which may be used in parallel for different purposes:

- MOsteoDD as a cheap and easy screening tool,
- DXA as a full scanner to be used for patients selected with MOsteoDD.

# 10. Appendix 3: Competition

**At present the following densitometric methods are used in the diagnostic process**[8]:

- **Roentgen Absorptiometry RA,**
- **Single X-ray Absorptiometry SXA,**
- **Dual X-ray Absorptiometry DXA,**
- **Quantitative Computerized Tomography QCT,**
- **Quantitative Ultrasonography QU.**

## 10.1. DXA

Dual-energy X-ray absorptiometry (DXA, DEXA) it is the most popular technique to measure bone density (BMD). Two X-ray beams with different energy levels are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Dual-energy X-ray absorptiometry is the most widely used and most thoroughly studied bone density measurement technology.

DXA scans are used primarily to evaluate bone mineral density. DXA scans can also be used to measure total body composition and fat content with a high degree of accuracy comparable to hydrostatic weighing with a few important caveats. However, it has been suggested that, while accurately measuring minerals and lean soft tissue (LST), DXA may provide skewed results as a result of its method of indirectly calculating fat mass by subtracting it from the LST and/or body cell mass (BCM) that DXA actually measures.

The World Health Organization has defined the following categories based on bone density in white women: severe (established) osteoporosis with T-score less than –2.5 and one or more osteoporotic fractures.

There are some variables in addition to age that are suggested to confound the interpretation of BMD as measured by DXA. One important confounding variable is bone size. DXA has been shown to overestimate the bone mineral density of taller subjects and underestimate the bone mineral density of smaller subjects. This error is due to the way by which DXA calculates BMD. In DXA, bone mineral content (measured as the attenuation of the X-ray by the bones being scanned) is divided by the area (also measured by the machine) of the site being scanned.

Because DXA calculates BMD using area (aBMD: areal Bone Mineral Density), it is not an accurate measurement of true bone mineral density, which is mass divided by a volume. In order to distinguish DXA BMD from volumetric bone-mineral density, researchers sometimes refer to DXA BMD as an areal bone mineral density (aBMD). The confounding effect of differences in bone size is due to the missing depth value in the calculation of bone mineral density. Despite DXA technology's problems with estimating volume, it is still a fairly accurate measure of bone mineral content. Methods to correct for this shortcoming include the calculation of a volume that is approximated from the projected area measure by DXA. DXA BMD results adjusted in this manner are referred to as the bone mineral apparent density (BMAD) and are a ratio of the bone mineral content versus a cuboidal estimation of the volume of bone. Like the results for aBMD, BMAD results do not accurately represent true bone mineral density, since they use approximations of the bone's volume. BMAD is used primarily for research purposes and is not yet used in clinical settings.

Other imaging technologies such as Computed Quantitative Computer Tomography (QCT) are capable of measuring the bone's volume, and are, therefore, not susceptible to the confounding effect of bone-size in the way that DXA results are susceptible.

DXA uses X-rays to assess bone mineral density. However, the radiation dose is approximately 1/10 that of a standard chest X-ray.

The quality of DXA operators varies widely. DXA is not regulated like other radiation-based imaging techniques because of its low dosage. Each state has a different policy as to what certifications are needed to operate a DXA machine. California, for example, requires coursework and a state-run test, whereas Maryland has no requirements for DXA technicians. Many states require a training course and certificate from the International Society of Clinical Densitometry (ISCD).

[8] Czerwiński E., Chrzan R.: Współczesne techniki obrazowania osteoporozy. Twój Magazyn Medyczny. Osteoporoza II, 8/2005, rok X, 8(157); 7-16

It is important for patients to get repeat BMD measurements done on the same machine each time, or at least a machine from the same manufacturer. Error between machines, or trying to convert measurements from one manufacturer's standard to another can introduce errors large enough to wipe out the sensitivity of the measurements.

DXA results need to be adjusted if the patient is taking strontium supplements.

The WHO committee did not have enough data to create definitions for men or other ethnic groups. Special considerations are involved in the use of DXA to assess bone mass in children. Specifically, comparing the bone mineral density of children to the reference data of adults (to calculate a T-score) will underestimate the BMD of children, because children have less bone mass than fully developed adults. This would lead to an over-diagnosis of osteopenia for children. To avoid an overestimation of bone mineral deficits, BMD scores are commonly compared to reference data for the same gender and age (by calculating a Z-score).

**DXA method is considered as costly and risky due to exposure to X-ray.**

As a rule medical devices because of their specific character are available through authorized dealers or directly from producers. Their price depending on the type and the equipment ranges from several to several hundred thousand PLN.

In the case of diagnostic devices using dual-energy X-ray absorptiometry it is necessary to add the cost of adapting a room where it is to be located, medical personnel salaries and spare parts cost that can reach ¼ of a device initial price. Stationary densitometers are purchased by hospitals and large health care centres. Portable devices are offered to smaller medical facilities.

Advertising and promotion which is directed to specialists concentrates on device parameters and emphasizes high degree of technological advancement as well as additional options such as possibility of transmitting the results via the Internet.

The most popular and representative diagnostic devices have been presented below.

## 10.2. Densitometric devices by Siemens – Norland medical systems

**XR 46** – Professional apparatus for diagnosing and treatment monitoring of metabolic bone diseases. It uses collimated X-ray radiation. Bone densitometer model **XR 46** measures bone density at the following sites:

- central skeleton (lumbar spine AP and Lateral; femur neck);
- peripheral skeleton (forearm);
- WHOLE BODY
- RESEARCH SCAN of an area chosen by a physician

- Possibility of animal bone analysis (Small Subject).
- The device is equipped with the option BODY COMPOSITION – analysing composition and mass of bone and soft tissue (SOFT TISSUE COMPOSITION).
- Device dimensions: 261 cm x 122 cm.
- High scan speed / minimal radiation dose:
  - Spine AP <1,5 min/< 1 mrem;
  - Spine Lateral <4 min/< 5 mrem;
  - Femur neck <2 min/<1 mrem;
  - Forearm <3 min/<1 mrem;
  - Whole body <5 min/<0,1 mrem
- Precision ~1%.
- Automatic elimination of high density areas (implants).
- Ionizing radiation strength active selection technology.
- Unique 77 point calibration system – precision of a measurement is regardless of patient's individual build.

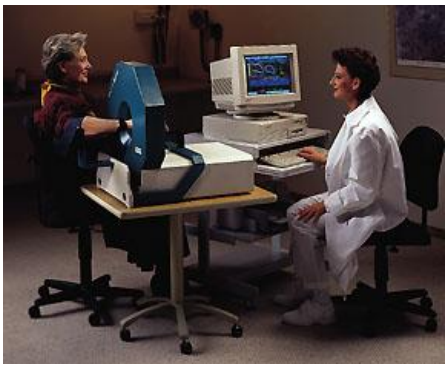
**EXCELL** – Smaller than **XR 46** bed densitometric apparatus belonging to **DEXA** family. It uses Pencil Beam technology (collimated X-ray radiation).


- Dimensions: 182 cm x 122 cm
- Table dimensions: 181 cm x 88 cm
- Shortened scan time for spine AP <1,5 min, and for femur < 2 min.
- Dose: < 1,0 mRem.
- Precision: 1 % – spine; 1,2 % – for femur.
- 77 point calibration system.
- Dynamic filtration.
- Reference base T-score and Z-score.
- Reference base for children from 2 to 20 years of age.
- FRACTURE RISK ASSESSMENT option.

## 10.3. Apollo™

is a densitometric apparatus belonging to DXA family**.** It is destined for screening and preliminary diagnostics of metabolic bone diseases. It enables to analyse metabolically active structure of heel bone cancellous tissue (Os Calcis). Apollo™ is characterized by a relatively low emission of ionizing radiation absorbed by a patient (< 0,2 mRem) and short measurement time (< 15 s). The device belongs to a so called "dry" apparatus group. The results are displayed on apparatus steering panel. The measurement is taken at the heel bone (os calcis), knee cap (patella) and phalanges. However, the results obtained measuring the heel bone and other skeleton areas are significantly different from spine and femur mineral density. So although the method is simple and relatively inexpensive, it can be recommended only as a preliminary screening exam that does not form the basis for pharmacological treatment.

## 10.4. XCT 2000



is one of the small size peripheral densitometric scanners. Peripheral Quantitative Computed Tomography (pQCT) has the ability to determine the real (volumetric) bone density of the forearm. XCT 2000 defines the radial bone core and sponge structure density selectively. Microscopic scanners belonging to the same group allow to reconstruct bone density with the resolution from 0.2 mm to 0.8 mm. Radiation doses of the densitometric scanner are comparable to those of DXA. The device allows to monitor the treatment within metabolically active sponge structure and enables early assessment of the therapy effects.

## 10.5. Densitometric devices by GE – Lunar series

**STATIONARY DENSITOMETER:**

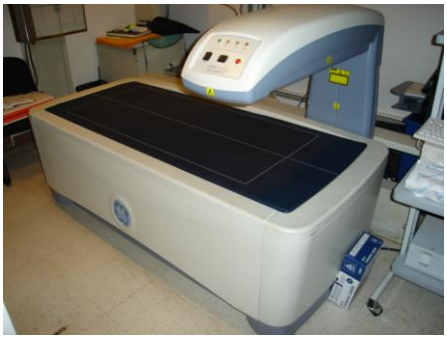
**DPX Duo**

- X-ray densitometer with a pencil beam.
- Scanning data: Spine AP – 90 sec., 0,020 mGy (<1% CV) Hip – 90 sec., 0,020 mGy (<1% CV)
- Scanning options: lumbar spine AP, hip, two hips, forearm, Total Body, Body Composition – with determining body composition within android and gynoid regions, lateral spine BMD, paediatric option.
- Technical options:
- DICOM, teledensitometry, multi-access (1–10 users), Dexter PDA interface, CAD (computer aided densitometry), SmartScanT (intelligent scanning) AHA (Advance Hip Assessment), programme for fracture risk assessment in 10 years.
- Dimensions (length x height x width): 187 x 128 x 104 cm, weight: 202 kg.
- Dispersed radiation: at a distance of 100 cm from apparatus axis <2 µSv/god.

**DPX Pro**

The device belongs to DEXA family (Pencil Beam- a narrowly collimated beam). The DPX Pro system is available in compact and full version. The DPX Pro device enables early diagnosis and treatment monitoring of osteoporosis both in the typical locations (lumbar spine, the femur neck) and in the sites such as the forearm and the whole skeleton. Total Body measurement option offers additional analysis of body composition determining body fat tissue distribution and muscle tissue. Fat tissue data are compared with reference data in a graph. The DPX Pro system is equipped with advanced software which enables to examine simultaneously both femur necks and automatically calculate their density mean value and parameters describing mechanical bone resistance and its susceptibility to fracture (HAL – hip axis length and CSMI – cross-sectional moment of inertia). Orthopaedic software allow to assess and monitor bone tissue mass around an endoprosthetic femoral stem. Lateral spine scans providing BMD assessment allow to identify deformations and vertebrae fractures, independent from BMD osteoporosis risk factor. High measurement precision and low ionizing radiation doses enable early skeleton state diagnostics even in children (paediatric application). DPX Pro software is equipped with OneScan and CAD options and thanks to a SmartScan™ system the apparatus has high precision (CV% < 1) and capacity (90 sec/exam). The software possesses numerous other options such as data base management and transmitting exam results via internal network or the Internet.

**PRODIGY ADVANCE**



The device is the most technologically advanced densitometric system by GE. It is a densitometer belonging to the DEXA family (narrowly collimated fan beam) which is a perfected version of Prodigy system. The densitometer is equipped with SmartFan™ technology and supports a physician-friendly software enCore™. Using a unique digital detection technology and a ground breaking software solutions has the ability to perform a precise measurement of the spine and the femur neck in 10 seconds! (QuickView™). PRODIGY ADVANCE system carries out the BMD analysis at different sites (lumbar spine, total body, palm, around endoprosthetic femoral stem) and will identify and classify the spine fractures and assess the mechanical resistance of the femur bone. PRODIGY ADVANCE system is equipped with all options in densitometry offered by Prodigy system including OneScan and CAD. There are also available options for research purposes such as Infant program and Small Animal Program. PRODIGY ADVANCE has 40% higher clinical precision in comparison with rival systems. The systems allows to compare the test results obtained using rival devices with the results of the exam carried out with PRODIGY ADVANCE densitometer. The software possesses a number of additional options for data management and results transmission via internal network or the Internet. Price: 299 500.00 PLN

**ACHILLES InSight** – allows to choose an appropriate analysis site at the heel bone (Os calcis) through imagining the examined bone in real time. Achilles InSight is an apparatus belonging to the group of ultrasound "dry" devices. Classic water-filled tube was replaced with membranes. The system does not require any additional equipment.

**SYSTEM ELECSYS® 1010/2010**

It is the first automatic method for osteoporosis markers detection in blood serum offering a quick, individual patients' diagnostics. (Certificate ISO 9001). It is extremely expensive and considered to be unstable by many researchers therefore it is largely used in scientific studies nowadays.