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Early Detection Techniques for Osteoporosis

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1. Introduction

Osteoporosis (OP) is a serious disease and its early diagnosis is very important at the right time. These days, there are some conventional techniques of the diagnosis of this disease but these techniques have their limitations and reliable information is not obtained at the initial stage of the disease. Therefore, a new technique for the detection of OP at an early stage is required to be developed. In the present chapter, a new technique, based on Micro Electro Mechanical System (MEMS) technology, will be discussed to overcome the limitations of earlier techniques.

In the present chapter, main emphasis is placed on the early detection of OP. New types of OP detection techniques, based on the biomechanical, optical and electrochemical principles, will be explained and compared to achieve an improved detection methodology for OP. A new amperometric immunosensor using gold nanoparticles and a novel microfluidics BioMEMS chip as a point of care testing (POCT) technique will be introduced for design, fabrication and characterization.

The chapter covers the study which has been mainly divided into three parts: basic measurements on physical, biomechanical, optical and chemical properties of normal and OP bones and serum; and design and development of amperometric immunosensor and BioMEMS chip. (Ahn C.H et al., 2004, Arnaud C.D et al., 1996 Atkinson, P.J. 1964, Auroux, P.A et al., 2002, Bakker, E., 2006, Berthounaud L, F., 2002, Bianchi, 2005, Ban C, 2004, Bal S.K, 2002)

An overview of OP research trends with the objectives of the research, and scope and significance of the study, is also presented. Causes and diagnostic techniques for OP will be reviewed in the beginning of the chapter.

2. OP detection & early detection of osteoporosis (EDO)

Since OP is most common among elder people, the overall costs to maintain the healthy body will most likely escalate in the near future. Hence to reduce the sufferings, the best solution is early detection (Bianchi, M.L., 2000, Blair, 2000). The early detection of disease states results in improved treatment outcomes, possibility of living longer a healthy life (Arnaud et al., 1996; Singh, 2006).

Early detection is possible by biomarkers or the "intervening phenotypes" in the biofluids like saliva, serum and urine which can be (a) surrogate measures of any malignancy in the bone;

(b) identifiers of inherited variations associated with disease susceptibility; or (c) "pre-disease" lesions that are highly predictive of subsequent disease (Becerra-Rojas & Jupari, 2001).

Diagnosis of OP at the right time can save from compressive treatments and immobility. Generally, in medical practice, identification of disease is based on recognition of symptoms and also testing specific features to confirm the presence of a particular disease. But for OP, it is hard to predict the disease as it silently creeps into the body with minimal symptoms of back pain, toothache and some hunch-over, etc. These initial symptoms point to the old age also and hence the unaware patient realizes this only after having a fracture in the bone. The unaware human when realizes about the disease due to some bone-fractures. In the hospital, anteroposterior and lateral X-rays of the special bone site are obtained to assess the presence of fractures, using the BMD measurements. Finally, they realize the presence of OP then the treatment becomes unaffordable and the patient becomes bed-ridden as shown in Fig. 2. Hence early detection of OP (EDO) is extremely necessary (see Table 1) with new devices like POCT (point of care technology) device using BioMEMS technology. Micro-fluidic chips are also playing key role to deliver new devices for better health care. The sensitivity and specificity of the POCT device would give earliest possible detection. Several promising directions for detection of bonemarker for OP have been interrogated (Arnaud, 1996; Singh, 2006, Singh, 2007, Singh, 2008, Singh, 2009).

Various researchers have studied OP disease for biological, chemically, physiological and engineering aspects in the past, by using different types of measurement techniques and methodologies (Arnaud, 1996; Korkia, 2002; Raiz, 1997; Singh, 2006). However, newer and newer techniques with new advances in technology, like micro/ nano technology, are being developed.

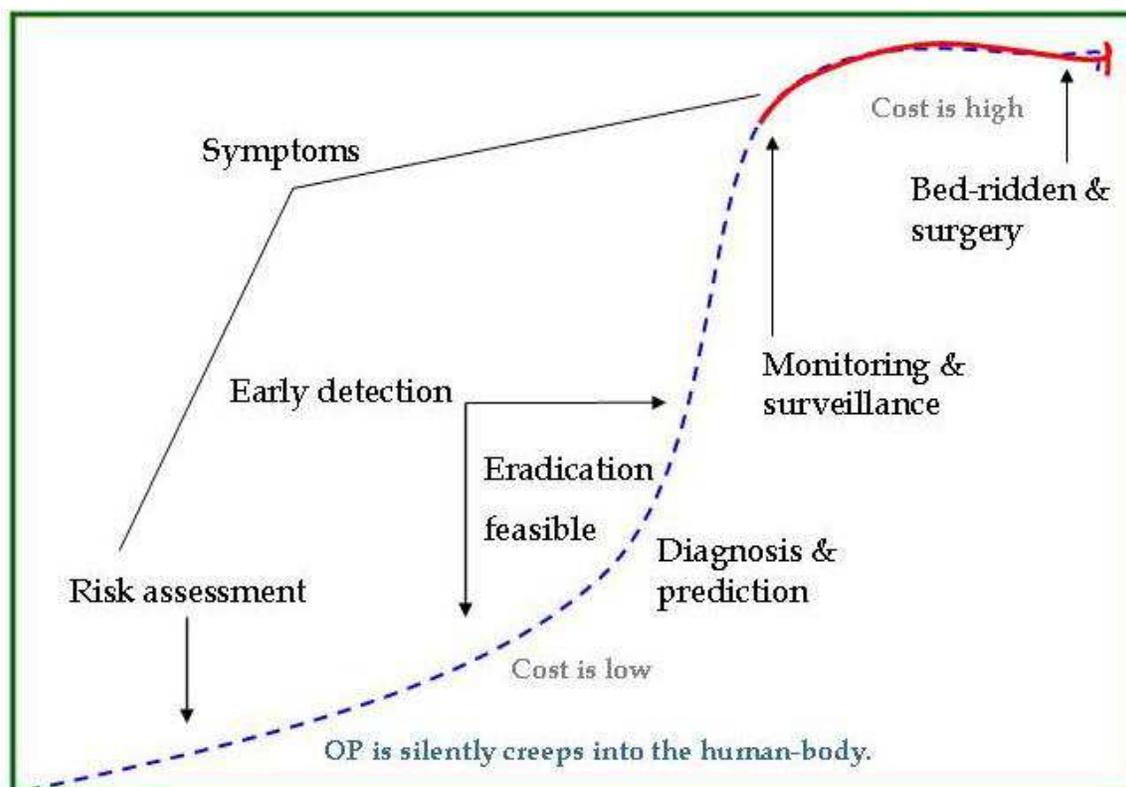


Fig. 1. Early Detection of OP (EDO)

S.No	Specification	Consequences
1	Early detection	Screening for large number of population
2	Minimal invasive	Uses only micro amounts of biofluids
3	Site-specific	Bone turnover specific bonemarkers
4	Diagnostics levels	OP-specific
5	User-friendly	Self testing is possible, easy to use
6	Simple, low cost	Portable, home care

Table 1. Importance of EDO(Singh, 2006)

3. Technical terminologies

3.1 Osteoprotegerin

Osteoprotegerin, also known as osteoclastogenesis inhibitory factor (OCIF), is a cytokine and a member of the tumor necrosis factor (TNF) receptor superfamily. It is a basic glycoprotein comprising 401 amino acid residues arranged into 7 structural domains. It is found as either a 60 kDa monomer or 120 kDa dimer linked by disulfide bonds.

3.2 Biological MEMS (BioMEMS)

It is a combination of a Micro-electromechanical system (MEMS) with the biological systems, like protein, DNA or cell. It includes micro- and nanosystems for genomics, proteomics, and drug delivery analysis; molecular assembly, tissue engineering, biosensor development, and nanoscale imaging (Singh et al., 2007, 2009, Vijayendran et al., 2003).

3.3 Microfluidics

Microfluidics is a multidisciplinary field comprising physics, chemistry, engineering and biotechnology that studies the behavior of fluids at the microscale and mesoscale, that is, fluids at volumes thousands of times smaller than a common droplet. It also concerns the design of systems in which such small volumes of fluids are used (Singh, 2007; Vijayendran et al., 2003).

3.4 Electrochemical sensor

The biosensor in which a biological process is harnessed to an electrical sensor system, such as an enzyme electrode. Other types couple a biological event to an electrical one via a range of mechanisms, such as those based on oxygen and pH (Heineman, 2001, Singh et al, 2008, 2009).

3.5 Immunosensor

Immunosensor uses the immuno-compounds (antibodies or antigens) as biological receptors configures the so-called immunosensors, which are usually the result of the integration in one device of an immunoassay and a directly associated transducer. The antigen-antibody complex formation can be detected either directly (without using any labeled compound) by certain physical (potential, capacitance, conductivity compound) measurements or indirect approaches in which one immuno-compound is conjugated with an indicator molecule (Bakker and Quin, 2006).

3.6 Spectroscopy

It is a non-invasive analytical technique with an infinitely broad range of applications, especially in medical field. This gives a non-destructive analysis. It helps in identification of

the elements and the elucidation of atomic and molecular structure by measurement of the radiant energy absorbed or emitted by a substance in any of the wavelengths of the electromagnetic spectrum in response to excitation by an external energy source (Chittur, 1998; Clark and Hester, 1996).

3.7 Lab-on-a-chip (LOC)

LOC is to integrate multiple functions on a single chip of only millimeters to a square centimeters in size and that are capable of handling extremely small fluid volumes down less than pico liters, LOC device is a sub-set of MEMS device (Chittur, 1998; Clark and Hester, 1996). The term "Lab-on-a-Chip" was introduced later on when it turned out that μ TAS (Micro Total Analysis System) technologies were more widely applicable than only for analysis purposes.

(<http://en.wikipedia.org/wiki/Lab-on-a-chip>).

4. Classification of OP detection techniques

There are several methods for detection of OP as shown in Fig. 2 (Singh, 2006).

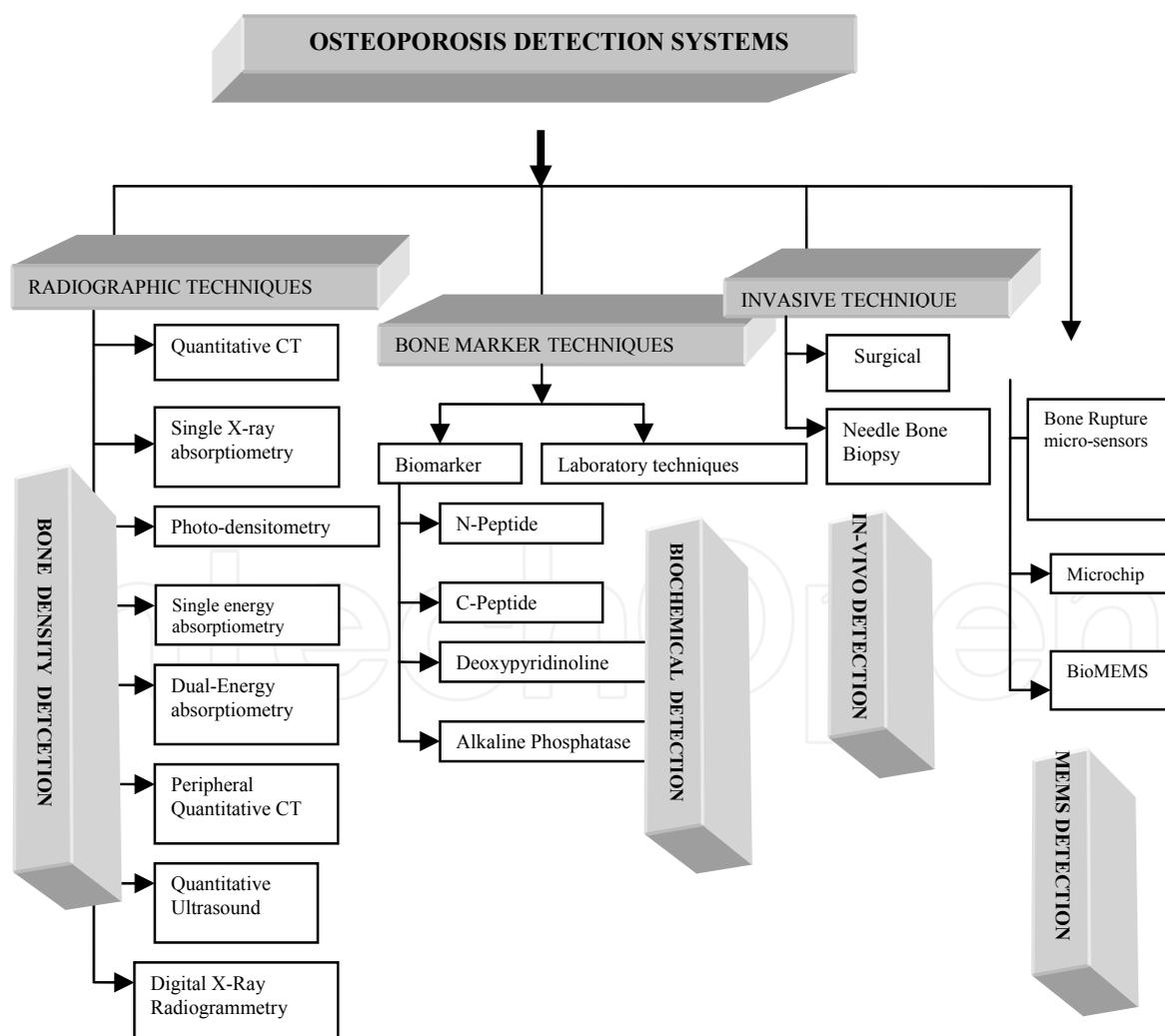


Fig. 2. Classification of Detection Techniques for OP (Singh, 2006)

4.1 Radiographic diagnosis

Radiogrammetry, a technique that has been in use for more than 30 years, relies on the measurement of the cortical thickness of bones in the hand (metacarpals) to estimate bone mass. This technique suffers from relatively poor accuracy and reliability and has largely been supplanted with new techniques (Bianchi, 2000)

The following diagnostic techniques are generally used for the detection of osteoporosis (Arnaud, 1996; Sartoris, 1996, Bianchi, 2005)

Bone Mineral Density Technique (BMD) is an effective approach for detection of osteoporosis. A decrease in the amount of bone, resulting in thin, weakened bones that are susceptible to fractures. Several techniques are available for BMD testing. For example; dual-energy X-RAY absorptiometry (DXA) remains the standard for testing the BMD. Dual energy absorptiometry measures the bone density within a given area of bone (g/cm^2). This technique offers the advantages of higher precision, minimal ionizing radiation exposure, rapid scanning time and the ability to access cortical and trabecular bone mass at appendicular and axial sites. Limitation, include equipment expense, the need for certified X-Ray technician and non-portability. In addition, DXA scans of the spine may show a false increase in spinal BMD in patients with osteophytes, aortic calcifications and degenerative arthritic changes.

The conception of osteoporosis relates bone health to bone strength, rather than mass. A bone's health implies that it should have enough strength to keep voluntary loads from causing spontaneous fractures. Thus, the diagnosis of osteoporosis would be a biomechanical matter concerning both bone strength and muscle strength (Martin et al., 1998). This supposes two kinds of problems, namely: (a) to properly assess bone material properties, structural design and strength; and (b) to correlate the respective indicators with suitable indicators of muscle strength. As a standard densitometry is unsuitable to assess muscle strength or bone strength, it should use of other, preferably cross-sectional analyses of bone structure as those provided by quantitative computed tomography (QCT), peripheral quantitative computed tomography (pQCT), MRI, or similar procedures. The value of pQCT lies in the ability of the software to account for all the 'mass', material and architectural factors in whose-bone strength and to provide data on muscle cross-sections (Burr, 1997, Boyle et al, 2003, Singh et al, 2006).

4.2 Quantitative CT

This provides the evaluation of trabecular bone density of the lumbar spine based on bone volume. Quantitative computed tomography (QCT) may be less practical than DXA because of the lower precision, higher cost and increased radiation exposure (Singh et al, 2006).

4.3 Peripheral bone densitometry

These devices used for many devices single-energy X-ray absorptiometry, peripheral DXA and peripheral CT. these device have the advantages of less expense, portable equipment, reasonable precision, and low radiation exposure. The use of quantitative ultrasonography for screening of osteoporosis and assessing fracture risk has increased. Using the speed of sound and broadband ultrasonic attenuation measurements, ultrasonic densitometry provides on bone elasticity and structure in peripheral sites. Advantages of this method, is low cost and lack of ionization radiation (Singh et al, 1997, 1998, 1999, 2006).

4.4 Single-energy absorptiometry

Single-energy absorptiometry measures bone mineral at peripheral sites such as the wrist and heel. Single photon absorptiometry (SPA) used a radioactive energy source, usually iodine-125 to estimate the amount of bone mineral at peripheral measurement sites. In recent years, Single-energy X-ray absorptiometry (SXA) has supplanted SPA for measurements of the peripheral skeleton (heel and wrist) because of its better reproducibility and ease of use. SXA avoids the necessity of obtaining and disposing of radioactive energy sources. It requires immersion of the part in water bath and hence can measure bone mass in peripheral bones like bones of forearm and legs (Singh et al, 2006, Blair et al, 2003).

4.5 Dual-energy absorptiometry

Bone density tests are painless, non-invasive and safe. Dual-energy absorptiometry was developed to measure bone in parts of the skeleton (lumbar spine, hip, and total body) that could not be measured with single-energy devices. Currently dual-energy X-ray absorptiometry (DXA) is the most widely used technique for measuring bone at these sites. DXA devices also are capable of measuring bone at the heel and wrist with high accuracy and precision, with very low exposure to radiation (Singh et al, 2006).

4.6 Peripheral quantitative CT (pQCT)

Quantitative computed tomography (QCT) measures the density of vertebral trabecular bone, the spongy bone in the center of the vertebra. pQCT devices are QCT instruments that have been adapted for measurements at peripheral sites such as the wrist (Singh et al, 2006).

4.7 Quantitative ultrasound (QUS)

Quantitative ultrasound devices measure bone at several skeletal sites, including the heel, hand, finger, and lower leg. The heel measurement it is composed of primarily trabecular bone, similar to the composition of the spine. Ultrasound devices based on the changes in the speed of sound (SOS), as well as specific changes in sound waves (broadband attenuation or BUA) as they pass through bone. QUS measurements provide information on fracture risk by providing an indication of bone density and possibly also information on the quality of the bone. Ultrasound devices do not expose the patient to ionizing radiation. Ultrasound devices do not expose the patient to ionizing radiation (Singh, 2006, Sartris, 1996)

4.8 Digital X-ray radiogrammetry (DXR)

Recently, the computer technology has renewed interest in this old technique. The Pronosco X-posure system estimates forearm bone mass from measurements of the cortical width of bones in the hand using computerized digital x-ray radiogrammetry from a single plain radiograph of the hand and wrist. The BMD estimate, referred to as DXR-BMD, is corrected for cortical porosity and striation. The results indicate that this technique is highly reproducible and appears to be at least as good as other peripheral bone assessment techniques in its ability to discriminate among patients with low bone mass at the spine and/or hip and osteoporotic fractures (Sartoris, 1996).

4.9 Photodensitometry

Previously, radiographic absorptiometry (RA) uses standard X-ray images of the hand and distal forearm are taken with a graduated aluminum reference. The radiographic image of

the hand and wrist is captured by a video camera and the levels of grey seen on the hand image are quantified and compared with the grey levels of the reference standard, resulting in an estimate of bone mineral density (BMD). The cortical thickness of the bones can also be measured. Radiographic photo densitometry comprises of comparing the optical density of bone X-ray with standard calibrative, aluminium-step-wedge. Although inexpensive and easily accessible, this method had poor reproducibility. Computer-assisted methods have reduced these errors and several commercial systems have been developed in recent years. Although RA is generally less precise than DEXA, radiographic absorptiometry holds promise as a cost-effective method to screen cases of osteoporosis. Further research is needed to evaluate its effectiveness in predicting fracture and monitoring therapy (Sartoris, 1996, Singh et al, 2006, Blair et al, 2006, Bouxsien and Mary, 2005).

4.10 Double photon absorptiometry

The principle of dual photon absorptiometry (DPA) is the use of a photon beam that has two distinct energy peaks. One energy peak will be more absorbed by soft tissue and the other by bone. The soft tissue component then can be mathematically subtracted and the BMD thus determined (Sartoris, 1996).

4.11 Neutron activation analysis

A limb is bombarded by slow neutron from a generator. This is taken up by the soft tissue to convert it into thermal neutron. This thermal neutron is captured by the nucleus of calcium ion. The nucleus becomes radioactive. Decay of the nuclei emits photon which can be measured by a Geiger counter, giving an idea of bone mass. This is reduced in osteoporosis.

(source: www.iupac.org/publications/pac/1995/pdf/6711x1929.pdf).

4.12 Biochemical techniques

Biomarkers are substances found in an increased amount in the blood, other body fluids, or tissues and which can be used to indicate the presence of osteoporosis. Biomarkers of bone remodeling (formation and breakdown), such as alkaline phosphatase and osteocalcin (serum markers) and pyridinolines and deoxypyridinolines (urinary markers), help in evaluating risk for osteoporosis. The research studies show that biomarkers correlate with changes in indices of bone remodeling and may provide insights into the mechanisms of bone loss which may give a basic detection method. The method may not be precise or accurate but it is quick, early, cheap and non-invasive way of detection. This method gives an indication of the onset of the disease (Sia, 2003).

4.13 Bone markers

There is a need for the development a non-invasive and repeated measurement of bone turnover which demands precision, accuracy and specificity. These kind of independent measurements of bone formation and resorption are done at organ or tissue level. The validated biochemical markers are urine and serum (see Table 2).

The two main biochemical markers for bone formation are serum alkaline phosphatase and serum osteocalcin. Markers for bone resorption include urinary calcium and urinary hydroxyproline: Alkaline phosphatase, which reflects osteoclast activity in bone, is measured in serum, but it lacks sensitivity and specificity for osteoporosis, because it can be

elevated or decreased with many diseases. It is increased with aging (see Table 2). Urinary calcium can give some estimate of resorption (loss of) bone, but there are many variables that affect this measurement. Urinary hydroxyproline is derived from degradation of collagen, which forms extracellular bone matrix. However, hydroxyproline measurement is not specific for bone, because half of the body's collagen is outside the bony skeleton. It is also influenced by many diseases, as well as diet. Several ELISA kits are developed by Osteomark Company for detection of Osteoporosis (www.osteomark.org).

S.No	Osteoblastic Activity	Osteoclastic Activity
1	S-alkaline phosphatase - Total alkaline phosphatase (S-tAP) - Bone alkaline phosphatase (S-bAP)	U-Hydroxyproline(U-OHPr)
2	S-osteocalcin(S-BGP)	U-collagen crosslinks - Pyridinoline(U-Pyr) - Deoxypryridine(U-D-Pyr)
3	S-carboxyterminal propeptide of human type I collagen(S-PICP)	S-C Terminal pyridine crosslinked telopeptide domain of type I collagen (S-ICTP) S-Tartrate-resistant acid phosphatase(S-TRAP)

Table 2. Urine and serum markers (Sartoris, 1996)

4.14 Laboratory methods

There are several preliminary tests to identify the loss of bone mass. A number of laboratory tests may be performed on blood and urine samples (Singh et al, 2006).

The most common blood tests evaluate:

- blood calcium levels
- blood vitamin D levels
- thyroid function
- parathyroid hormone levels
- estradiol levels to measure estrogen (in women)
- follicle stimulating hormone (FSH) test to establish menopause status
- testosterone levels (in men)
- osteocalcin levels to measure bone formation.

4.15 Needle bone biopsy

Needle bone biopsy is not a very common assessment technique of bone density. This test has limited availability, and is best utilized as a research technique for analysis of treatment regimens for bone diseases. The best clinical use of bone biopsy combines double tetracycline labeling to determine appositional bone growth and rule out osteomalacia. Doses of tetracycline are given weeks apart, and the bone biopsy is embedded in a plastic compound, sliced thinly, and examined under fluorescent light, where the lines of tetracycline (which auto fluoresce) will appear and appositional growth assessed (Singh et al, 2006).

5. Recent novel techniques

Osteoporosis is the disease which creeps into one's body silently without showing a significant symptom. The nature of the disease asymptotic until a gross deformity occurs in one's body. This is can be very serious and deadly for the patient. The time the patient realizes structural support of the body has totally deteriorated. The diagnosis and treatment is sometimes unaffordable for a common man. The patient has the control over prevention of this disease or is reliable, easy and cheap way is available for such deadly disease than proper care can be taken. There are several researches going on in order to achieve some cheap, easy early detection of osteoporosis (Singh et al, 2006). The latest trend is in miniaturizing the device which make it portable, useful for homecare, user-friendly, cheap, Non-invasive and provides a kind early indication for OP. This technique is based on MEMS based technique.

5.1 Bone fracture detection micro-sensor

The method for detection or investigation of osteoporosis is with the help of a micropump (Yung et al, 2004). The micropump has been designed using the electromagnetic principle to actuate the piston in two directions. A closed loop system is used for circulating the fluid with the pumping device. This is kind of pump is useful for blood sampling or drug delivery. Here the oscillating micropump is used to study the mechanosensitivity of bone cell for better investigation of osteoporosis. There is another research which has proposed an implantable, telemetry-based MEMS bone sensor (Singh et al, 2003, 2009) with the capability of determination of bone stress via wireless RF interface. The bone stress is detected using the embedded piezoresistive strain gauges with polysilicon layer and a CMOS chip (Singh, 1997).

Another design of micro-fabricated strain gauge array is used to monitor bone deformation *in vitro* and *in vivo* for detection of osteoporosis. These kinds of microsensors provide a map of distributed strain data over the area of interest on the surfaces of bone to monitor the structural integrity of bone. This type of strain membranes are wireless and implantable embedded in flexible membrane. A simulation experiment was conducted to develop such micro-strain gauge for study of osteoporotic bone (Yang et al, 2004).

A bone sensor has been used for the piezoelectric BioMEMS. An attempt has been made to develop bone-based piezoelectric sensors to detect the stress in bone (Singh, 2003). Another micro-scale sensor for bone surface strain measurement is discussed. This kind of sensor is used for studying the structural effects of osteoporosis. Designs and simulation using ANSYS finite element modeling tool of thin-film metal strain gauge. Metal films for electrical interconnection encapsulated in PDMS have been studied. The PDMS membrane was characterized to facilitate encapsulation designs. The basic fabrication steps like silanization, PDMS preparation, photolithography, PDMS metallization, wire bonding and finally device separation. With experiments were performed for optimizing and characterizing the device like mechanical testing, electrochemical testing and adhesion testing (Yang et al, 2004), and there is a new design which has been discussed here.

Another latest technology is detecting osteoporosis with the study of the brittleness of the bone. The bone mass and bone density play an important role in bone strength. It is

important to measure the brittleness or fragility or the bone mechanics. Certain walking studies are done and it is found that as the heel strikes the ground it creates force pulse, energy that passes up through the body and it is absorbed by bone. The osteoporosis reduces the quality of the bone so by attaching the skin-mounted sensors for measuring the electrical pulses of the muscles which is an active part of the skeletal system. If the person has osteoporosis the energy which passes up to the body is disrupted due to porous nature of the bone (<http://www.uc.edu/news/NR.asp?id=3280>).

5.2 Microfluidic channels – Detection by biomarkers

The total Alkaline phosphatase (AP) is the mostly widely used bone marker in the clinics and hospitals. AP have physiological substrates which splits the inorganic phosphatase with organic phosphatase, increasing the calcium-phosphatase product and enabling mineralization. AP is essential for normal mineralization of the bone. Bone AP (bAP) constitutes approximately 50% serum AP and the serum has the half-life of 24-48hrs. Though the half-life is relatively large but it may differ on cardiac rhythm, with peak levels in afternoon and night. The exact metabolic pathway is unknown. AP is measured with the help of spectrophotometer using p-nitrophenylphosphate as substrate. The bone and liver AP may be separated by electrophoresis but this method is time consuming and gives semi-quantitative results. The concentration of bAP concentration may be measured using two antibodies with small differences in affinity toward the isoforms (Singh et al, 2006).

MEMS based detection with alkaline phosphatase has been attempted by Kang and Park (2005). A microfluidic device has been used for enzyme assay. The measurement of enzyme-substrate reaction will do the substrate consumed. A lab-on-a-chip (LOC) device is developed for controlling the flow containing small volumes of liquids in microchannel which can speed up and simplifies sample preparation steps in LOC which offers high throughput, low version of traditional research. The microfluidic device is fabricated by the casting process with PDMS. It consists of three parts part I is the injection system, part II is the reaction chamber and part III is the microchannel. This particular microchannel measures the ALP activity using a micro-plate reader. Microfluidic mixing for single enzyme assay was applied and with mathematical prediction the enzymatic (Singh et al, 2006).

5.3 Biochemical based BioMEMS chip

A novel BioMEMS chip, based on gold nanoparticles, for the detection of osteoproteogelin (OPG). This biochip is used to evaluate the bone conditioning which is directly related to the diagnosis and prognosis of the osteoporosis, in an effective manner. The flow visualization of the mixing capabilities are characterized using micro-scale laser-induced fluorescence (LIF). The BioMEMS chip detection is based on competitive immunoassay. The monoclonal OPG antibody (anti-OPG) is immobilized onto the AuNPs deposited conducting polymer, using covalent bonding with a carboxylic acid group. The catalytic reduction is monitored amperometrically at - 0.4 V versus Ag/AgCl. The linear dynamic range is between 2 to 24 ng/ml with the detection limit of 2 ng/ml (Singh et al., 2007). Fig. 3 depicts schematic of the microfluidic chip.

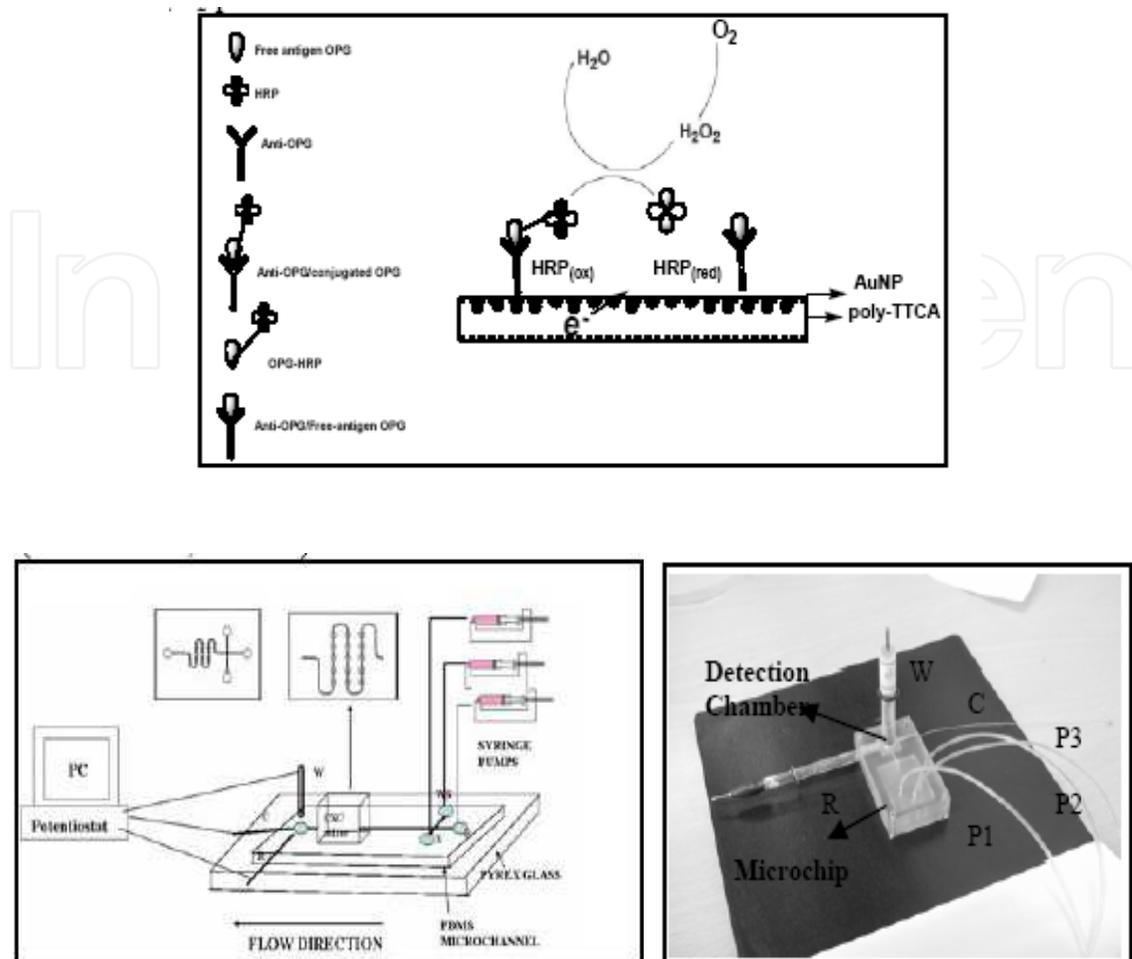


Fig. 3. Microfluidic technique for early detection of OP(Singh et al., 2007 & 2009)

Bone Formation	Bone Resorption
<ul style="list-style-type: none"> • Osteocalcin (OC) • Bone-specific alkaline phosphatase (BAP) • Amino terminal propeptide of type I collagen (PINP) • Carboxy terminal propeptide of type I collagen (PICP) 	<ul style="list-style-type: none"> • Pyridinoline (Pyr) • Deoxypyridinoline (dPyr) • Amino terminal telopeptide of type I collagen (NTx) • Carboxy terminal telopeptide of type I collagen (CTX)

Table 3. Biochemical Indices (Singh et al., 2006)
 (<http://www.scielo.br/img/revistas/abem/v50n4/31869t2.gif>)

5.4 BioMEMS-based sensors

BioMEMS using electrochemical immunoassay with microfluidic system (Heineman et al, 2001) help in blood sample analysis using the heterogeneous immunoassay. Two concepts of immunoassay are studied in this research. First is based on analogous microcapillary

immunoreactor and other combines the reaction and detection chamber within the area of electromagnet. Both are MEMS based system for alkaline phosphatase study.

Another MEMS microvalve with PDMS diaphragm and two chambers with thermo-pneumatic actuator for integrated blood test system with silicon have been suggested for point of care device. The blood test system can be reduced to reasonable cost with MEMS technology (Singh, 2006). The microvalve with long stroke has been fabricated with two chamber thermo-pneumatic actuator.

5.5 Spectroscopic techniques for early detection of OP

Optical techniques such as Fourier Transform Infrared Spectroscopy (FTIR) and Ultra Violet Visible Spectroscopy (UV-Vis) are employed to find the bone markers with an emphasis on the noninvasive modalities for early detection of osteoporosis. Blood plasma samples procured from two groups, patients and healthy persons were tested. Both of the optical techniques revealed obvious differences in the spectra; between two groups, for example, increase in intensity for OP persons. New peaks were found at 1588, 1456 and 1033 cm^{-1} in FTIR spectra, as shown in Fig. 4. On the other hand, in UV-Visible spectroscopy results, a new peak appeared in the OP patients' spectra at the wavelength of 420 nm, as shown in Fig. 5. These differences in the spectra of the two types of samples, allow rapid and cost-effective discrimination of the potential patients with the optical techniques which were verified by the bone densitometer in the hospitals. The new technique used here is quick, reliable and effective.

A hierarchical algorithm is used to investigate and quantify the mutual relevance between successive clusters in terms of heterogeneity values as shown in the Fig.6.

Fig. 6 represents the classification with the spectra at 1539-1542 cm^{-1} . This gives clear distinction between the patients and healthy groups for the amide II group.

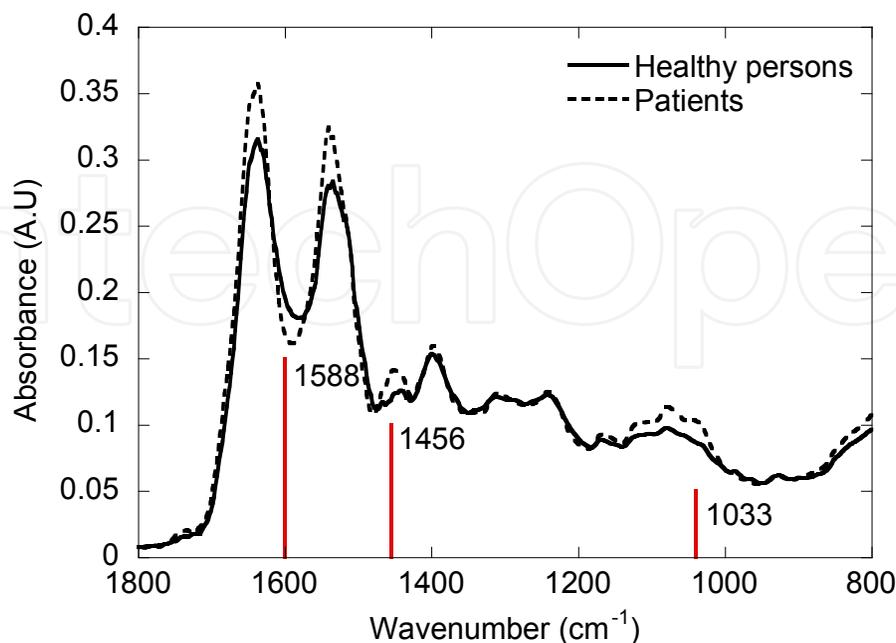


Fig. 4. FTIR results for EDO (Singh et al., 2010)

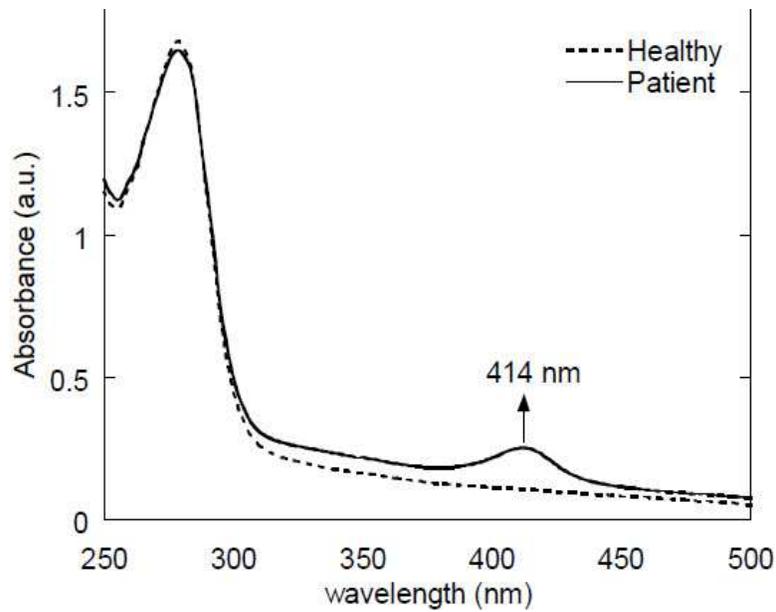


Fig. 5. UV-visible spectroscopy for EDO (Singh et al.,2010)

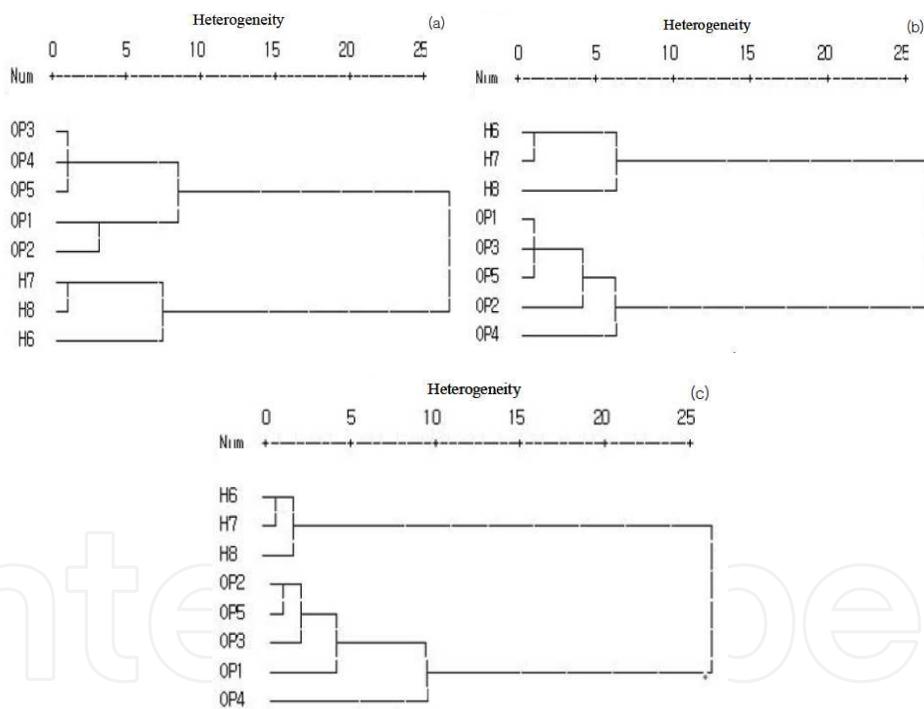


Fig. 6. Cluster analysis(Singh, 2010)

6. Discussions

6.1 Bone density testing

There is several bone density measurement testing techniques which have been discussed with their working principles. The recent developments in the instruments for BMD measurement have also been discussed. But there are several limitations in these devices. The testing with these devices is very expensive, early detection is not easy, these are invasive measurement, errors in magnification may occur, accuracy is not achievable, scan time is high, harmful

radiation may cause problems in the body, home care is not possible and the instruments are not portable. Specially trained persons are required to operate such sophisticated equipments. Though BMD measurement is the most accurate method for detection of Osteoporosis but it is unable to help in early detection and is very expensive. Early detection of such a silent and deadly disease is important for the mankind. Hence there is a need for new, novel, portable, cheap detection systems to be developed for point of care testing.

6.2 Invasive technique

The invasive technique has several risks involved like skin is punctured. There is a slight chance that the needle may cause fracture the bone being sampled or injure one of the nerves, blood vessels, or organs near the biopsy site. If complications occur, another surgery may be needed to treat the problem. After a bone biopsy, there is a slight chance that the bone may become infected, osteomyelitis or not heal properly. In rare instances, the bone from which the biopsy sample was taken may become weak and break, fracture at a later time. This type detection is only good for extreme severe cases.

6.3 Biochemical measurement

There are several bone markers or the biomarkers available for the early detection of the osteoporosis which control the osteoblastic and osteoclastic activity. The biochemical detection is not accurate detection but it gives the indication for onset of osteoporosis detection.

6.4 MEMS-based techniques

The MEMS-based techniques are portable, handheld, easy to use, can be used for home care and point-of-care testing. But the accuracy of the detection may be achieved by using bone mineral density testing (BMD) (Singh et al., 2009, 2010).

7. Conclusions

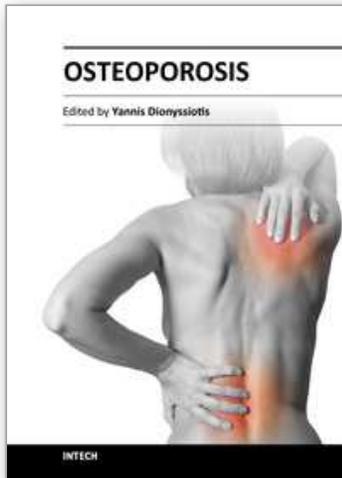
The radiographic techniques are needed for the accurate detection of osteoporosis as they give precise data for detection of the deadly disease. Generally, the patients are just unaware of the disease as osteoporosis creeps silently within a human body. Osteoporosis is a silent killer and is a very progressive disease. The time the person realizes the detection and treatment becomes unaffordable for patient. This research paper focuses on the urgent need for the development on early, non-invasive, cheap, and handheld POCT device for such a dangerous disease. These characteristics can be achieved by using a micro-size (MEMS/ Nano based techniques). There have been several attempts in this direction as mentioned in the paper above. But this area needs more of research and deep studies.

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Osteoporosis is a public health issue worldwide. During the last few years, progress has been made concerning the knowledge of the pathophysiological mechanism of the disease. Sophisticated technologies have added important information in bone mineral density measurements and, additionally, geometrical and mechanical properties of bone. New bone indices have been developed from biochemical and hormonal measurements in order to investigate bone metabolism. Although it is clear that drugs are an essential element of the therapy, beyond medication there are other interventions in the management of the disease. Prevention of osteoporosis starts in young ages and continues during aging in order to prevent fractures associated with impaired quality of life, physical decline, mortality, and high cost for the health system. A number of different specialties are holding the scientific knowledge in osteoporosis. For this reason, we have collected papers from scientific departments all over the world for this book. The book includes up-to-date information about basics of bones, epidemiological data, diagnosis and assessment of osteoporosis, secondary osteoporosis, pediatric issues, prevention and treatment strategies, and research papers from osteoporotic fields.

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