CHAPTER -1
Introduction

Biomaterials are materials that are used in medical devices or are in contact with biological systems [1]. They can be synthetic or naturally occurring and are solid or sometimes liquid. The study about biomaterials is called biomaterial science. Biomaterials encompass various fields like medicine, biology, chemistry, tissue engineering and material science. In laboratory they can be chemically synthesized by using metallic components, ceramics, polymers or different composites. Natural biomaterials are the proper materials of choice for repair of any damage inside body because they contain cells similar to the native tissue they are replacing along with many of the natural elements needed for proper tissue reconstruction. Our study includes three natural biomaterials, bone marrow of rabbit, tibia bone of rabbit and plasmacytoma eye lid tumor (male). Bone marrow is a natural biomaterial which is a very soft flexible tissue that lies within the hollow interior of long bones. It contains cellular components and matrix elements. This marrow is mainly responsible not only for new bone formation but also for fracture healing. Bone is also a naturally occurring composite biomaterial. It contains about 60% minerals, 10% water and 30% collagenous matrix [2]. Bone has at least four main functions.

- It provides a structure against which movement of muscles takes place and other organs of the body maintain their relative positions.
➢ The second one is that it is rich in minerals like calcium and phosphate and is a storehouse of them for the whole body.

➢ Thirdly, it provides protection to other vital organs inside the body.

➢ It helps to develop immune system by providing milieu (via bone marrow) [3].

In day to day life, bone gets broken down and regenerated. Bone regenerate itself in response to injury as well as in the development process from childhood onwards. It also remodels itself when the need arises [4-5]. The regeneration process consists of a well managed series of events. Bone induction and conduction processes are involved which include many intracellular and extracellular molecular-signaling pathways. The skeletal function is largely restored [5-6]. Fracture healing is a very common type of regeneration of bone. During this process pathway of normal fetal skeletogenesis, including intramembranous and endochondral ossification, is recapitulated [7]. In this process, scar tissues are not formed during healing. The bone is regenerated with restoration of its normal properties. The new bone formed is practically indistinguishable from the nearby healthy bones [5]. However in some cases, this regeneration process may be impaired; for example up to 13% cases of fractures in tibia do not recover completely [8].

Bone fractures have to be treated but the cost of such treatment is sometimes very high. So, it has prompted researchers to develop non-invasive methods. Stem cells of the marrow act as the progenitors for osteoblasts [10-12]. Autologous (own) bone marrow injection to fracture site is also a good method for fracture treating [13-15]. Helium-
Neon laser irradiation along with autologous bone marrow caused more hastened healing of the bone due to deposition of bone matrix and increased vascularization. Now-a-days electron beams in mega electron volt (MeV) range are used in radiotherapy for treatment of cancer by using Modern Linear Accelerators (LINAC). Same electron beam irradiation technologies have long been used for biomaterial applications in different fields [16]. It has been proven that the injection of bone marrow cells near the fracture area accelerates the fracture healing process of bone [17]. It contains mesenchymal stem cells that are able to form bone and cartilage and also enhance the osteogenesis in fracture healing [12-13]. Again, injection of bone marrow with low power laser irradiation also accelerate the fracture healing or bone binding process [18-19]. Appearance of altered osteoblast activity at the fracture site reflected by alkaline phosphate activity confirms this[20]. More calcium is accumulated also due to laser irradiation at fracture region [21]. The irradiation also causes increase in recombination (of biomolecules) density among the cells at the fracture site.

The majority of the bone is made of the bone matrix. It is composed primarily of inorganic hydroxyapatite and organic elastic protein called collagen. The MeV electron beam is a high energy charge particle beam. When the fracture site is irradiated with such electrons along with autologous bone marrow, more energy will be deposited at the site of irradiation because energy loss of electrons in a medium will be more than lasers. So it can be expected that the healing process should become faster as compared to low energy laser therapy. Such high energy electrons are available as output beams from a linear accelerator (LINAC).
LINAC is a device which can produce both high energy electron (MeV) and X-ray photon (MV) beams. Linear accelerating structure is used for accelerating ions and electrons in the LINAC. Acceleration employs electric and magnetic fields to accurately focus and steer the particles. These fields exert forces only on charged particles but no force on particles with no charge. Their energy is measured in eV which is the gain of energy of a particle having unit charge upon acceleration through a potential difference of one volt. For particle energies in the MeV range radiofrequency (RF) linear accelerators are used. In these devices, oscillation frequency of electric and magnetic fields is in the radio frequency range [22]. In such LINACs, energy from RF source is given to confined cavity to produce very high electric or magnetic fields. This cavity is bounded by a conducting material like copper which prevents the radiation loss of this energy. After passing through various stages of accelerator, a monoenergetic beam emerges out from the accelerator [23] which can be used for various purposes. Outcome of this radiation from LINAC is directly related to the accuracy of beam data used for clinical and other scientific research applications [24].

The interaction of radiation (electron beam) with matter shows various effects. The radiation induced effects in biomaterials include recombination of microorganisms, elimination of microorganisms associated with spoilage and contamination, sterilization of medically important proteins without affecting them and many more. “Radiation processing” refers to changing the material properties after exposing them to radiation. During passage of radiation inside matter, chemical bonds are broken and a new
material is created. Applications of electron beam irradiation include cross linking or recombination of microorganisms to improve or provide unique properties of biomaterial systems like other materials.

X-Ray photon beam radiation therapy is used to shrink tumors and kill cancer cells. The radiation may be delivered by a LINAC outside the body and is known as external beam radiation therapy. In radiation therapy DNA of the malignant cells are damaged and so also the cells [25]. It is done either directly or by creation of free radicals which can damage DNA. Such cells with their DNA damaged cannot continue further cell division and die. The dead cells are broken down by the natural process of the body. Now-a-days conformal radiotherapy (CRT) is the treatment of choice for various types of cancers. CRT is a type of external beam radiation therapy which is possible due to a specialized device attached with LINAC called a multi-leaf collimator (MLC). CRT allows higher doses of radiation to be given to the tumor area. The surrounding normal tissue and critical structures receive less radiation which can minimize the chances of side effects during radiotherapy and thereafter. This procedure is especially useful if the tumor is close to important organs or body structures and high doses of radiation are required to be given with minimal risk to healthy tissues.

Scope of the work

The necessity and high cost of treating bone fractures have forwarded the new research work of non-invasive methods of assessing fracture risk and prevention. Many works have been done in this field but all are long time consuming procedures. Irradiation by
MeV electron beams is expected to give better accumulation of bone matrix than other irradiation processes. Hence, there is an urgent need of such type of study for quicker bone healing/binding procedure. In the present work, we plan to treat bone fracture by MeV electron beam irradiation. For this purpose, the modern LINAC with vertical beam line arrangement installed at Hemalata Hospital and Research Centre, Bhubaneswar, has been used.

- A complete set of measured data of a commissioned LINAC for clinical and research applications are to be obtained.
- Irradiation of liquid samples with vertical beam line arrangement poses a few challenges. This has to be done in liquid nitrogen environment. For this purpose, a special type of attachment is required. We have designed and fabricated an instrumental attachment for this purpose which can hold liquid samples at liquid nitrogen environment.
- The study will be helpful for confirmation of MeV electron beam dose for rabbit bone marrow material modification.
- This study will generate a set of XRD & FTIR spectral analysis data for MeV electron beam irradiation of rabbit bone marrow.
- This will also help to find out the presence of bone forming elements (if any) at the fracture site after MeV electron beam irradiation.
- Our study also includes another biomaterial plasmacytoma (eye lid tumor). It
is a rare entity belonging to the category of non-Hodgkin lymphoma. It is a plasma cell disorder tumor. This disease was supposed to be treated by conformal radiotherapy with fine control of photon beam intensity. But eye lid is a very irregular surface and so it will be difficult to deliver adequate dose at the disease site safely. For this purpose a tissue equivalent material called Wet Cotton Bolus has been designed.

**Objectives**

- To tabulate a complete set of measured data of a commissioned LINAC for clinical and research applications.
- To design a special type of attachment to be used with the LINAC called liquid irradiation cell to work at liquid nitrogen temperature environment which can be used for all types of liquid samples for irradiation.
- Confirmation of MeV electron beam dose for bone marrow modification.
- Identification of different organic and inorganic materials present in bone marrow after MeV electron beam irradiation by XRD & FTIR spectral analysis techniques.
- Assessment of bone matrix elements developed at fracture site after MeV electron beam irradiation.
- Confirmation of the stage of bone fracture healing by clinical examination and weekly radiological studies of the fracture site.
• To develop a method about the fine control of MV photon beam intensity for using an indigenously designed Wet Cotton Bolus on tumor site.
References


