APPLICATION OF ILU-TYPE ACCELERATORS FOR STERILIZATION PURPOSES

A. A. Bryazgin, S. A. Maximov, V. E. Nekhaev, A. D. Panfilov, V. O. Tkachenko, A.F. Tuvik, L.A. Voronin, V.L. Gorbunov, Shtarklev E., Korobeinikov M.V. BINP, Novosibirsk, Russia

Abstract

In the report the review of existing methods of sterilization of medical products is submitted. The advantages of industrial accelerators in radiation technologies of sterilization are given. BINP works and results of researches on sterilization and producing of medical goods at accelerators ILU series are described. Most of investigations were spent in collaboration with various organizations.

INTRODUCTION

The primary electron accelerators used for sterilization were mostly scientific or laboratory machines than industrial machines. They possesses enough low electron energy (< 2.0 МэВ) and small power (< 5-10 kW). Besides they were unreliable, complicated in operation and service.

Nevertheless, the advantages of radiating methods of sterilization have become incontestable.

In the beginning of 70th abroad companies (Varian Associates, Phillips, Siemens) and NIIEFA, BINP in the USSR have developed the first linear industrial accelerators distinguished for durability and reliability.

At the present moment progress of accelerating engineering has resulted in occurrence various types of industrial accelerators for sterilization (LINAC by Titan, Siemens, BeamOne, Steris, NIIEFA etc., RODOTRON by IBA, ILU by BINP etc.) [2,3].

COMPARISON OF EXISTING METHODS OF STERILIZATION

Last years the appreciable rise in manufacture of disposable medical products such as syringes, surgical sets for operations, bed-clothes, etc. is observed. Because of specific materials of such products the only low-temperature sterilization methods are applicable.

Ethylene-oxide sterilization

In this method preliminary humidified medical goods are operated on gas in the tight chamber within several hours. The number of parameters of process such as humidity, pressure, temperature, concentration of gas, time of processing must be under control. The processed products should undergo aeration in the conditioned during several days for removal of the gas rests. Reliability of sterilization proves to be true by biological tests, time of testing also demands about 5-7 days. Relative process complexity and carcinogenic properties of ET results in gradual refusal of this method.

Sterilization at isotope source (Co - 60)

In due time (approximately up to middle of 70th) this method was rather popular, and the number of sources in the world was increased. Some factors leads to resign of using this method. Activity of Co-60 permanently decreasing (on 50 % within the first 5 years of operation), that makes necessary periodic "re-loading" of a source. The cost of split materials continues to be increased and now is about 2 USD for 1 Ku. Totally is about 40 % of radiation may be utilized (because of unique geometry of a radiation source). Time of Processing time to irradiate a production lot needs some hours. Enough long irradiation time results to partial degradation of goods and changes them color. At last, consumers are afraid of all connected with radioactive materials a little. It is necessary to add that the standard source of 1.0 MKu is equals in productivity to enough modest accelerator of 2.5 MeV, 15 kW.

Other methods

Among other methods we can name steam sterilization the plasma sterilization. The first method practically is not already using. By some data (for example, in Europe) the products sterilized with this method are forbidden for sale. The method of plasma sterilization provides superficial sterility only and is developing.

Sterilization at electron accelerator

In this method sub-light accelerated electrons with an energy from 2.5 up to 10.0 MeV and beam power from 1.0 up to 100 kW are used. They have sufficient penetrating ability for sterilization of medical products directly in retail containers.

Interaction of an electron beam with microbiological objects inside of contaminated product occurs in two ways:

- radiation directly ionizes atoms of DNA chains, irreversible damages them and thus interferes with duplication of microorganisms;
- radiation forms secondary particles and free radicals that injures a cells of microbes.

In comparison with ET electron treatment has the following advantages: high speed of technological process; there is no need to wait after the end of processing; the only one critical parameter is for permanent control - the dose received by product; safety of process; there is no necessity to use special "breathing" product packs.

In comparison with isotope sources electron treatment has the following advantages: high speed of processing;

time of an irradiation is short, i.e. degradation effects of a product material are much less expressed; the necessary dose is defined by only several parameters of the accelerator - energy, a current, scanning width; there is no necessity in "re-loading" of a source - the accelerator works tens thousand hours without deterioration of parameters; safety – when accelerator is switched off the radiation is completely absent.

The comparison carried out above allows to make a conclusion on appeal of radiating methods of sterilization. In turn, rather low cost of the equipment and low working costs determines the advantages of accelerating engineering in comparison with isotope radiation sources.

PROCESSING BY AN ELECTRONIC BEAM

For more than 25 years of development of electron accelerator ILU-type (pulse linear accelerator) are used in radiation-technological processes of laboratory, semi-industrial and industrial scale. Most widely they are used for an irradiation of PE isolation of a wire, by manufacture of thermoshrinkable tubes, for an irradiation of a film and a tape. These processes will be carried out at electron energy 1 - 2,5 MeV at power of an electronic beam up to 25 kW.

ILU applications in these areas of technology now extends, however, most intensively electron accelerators ILU type will penetrate into process of sterilization of single-use medical products and processes similar with sterilization. Such processes are, for example, decontamination of vegetative medical products and food additives.

For processes of sterilization and similar processes the accelerator ILU-10 with electron energy up to 5 MeV is developed at power of a beam up to 50 kW and are developed multi-resonator accelerators like ILU-12 and ILU-14 with energy of a beam of electrons from 3,5 MeV up to 10 MeV at power of a beam up to 100 kW.

Accelerators to ILU-12 and ILU-14 during sterilization and similar processes can be used both in an electronic mode and in a mode of “bremsstrahlung”.

THEORETICAL ASPECTS OF AN IRRADIATION

The overall performance of a radiation-technological installation (RTI), in particular, productivity, is defined by such parameters of the accelerator as energy and a current of a beam. Energy determines the depth of penetration electrons in substance (i.e. roughly speaking, thickness of a processable material), the current conditionally defines speed of passage of production through a zone of an irradiation. Purchase by a product of new properties (in case of updating of polythene) or sterility (in case of disposable medical clothes and food additives) is determined by a *dose* of radiation.

On Fig. 1 for various electron energy the distributions of doses on depth of an irradiated material are shown. Than energy is higher 10.0 MeV are forbidden for use in practice of sterilization because of probable occurrence of the induced radio-activity in an irradiated material. An abscis axis is graduated in terms of the *mass thickness* determined as d=m/S (in g/sm^2). This value is calculating on the assumption of weight and the surface area of an irradiated product (or packings with products).

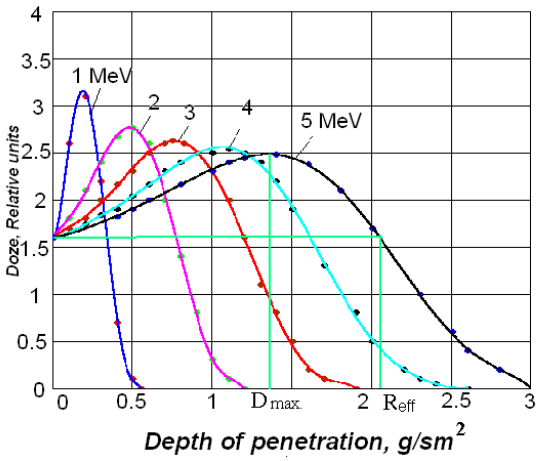

Figure 1:. Dependence of the dose on depth of penetration.

Apparently from diagrams Fig.1, prominent features of interaction electrons with substance results to that the dose in depth of substance Dmax always is more a than dose on surface Dmin. For Dmin minimally necessary sterilizing dose, for medical products, as a rule, laying in a range 25-35 kGr usually is accepted. For *effective depth* Reff. of penetration of electrons depth on which the dose is equal to a dose on a surface is accepted. Therefore at a unilateral irradiation and thickness of packing no more Reff. the significant part of beam power (which, as a matter of fact, there is an area under a curve of dose distribution) is lost, that, certainly, reduces productivity of installation. For avoidance of these losses the two-side irradiation is usually used.

In case of commercial use of RTI the definition of its productivity is the crucial factor.

Is simple enough to estimate productivity of installation at a two-side irradiation of production homogeneous or close to homogeneous weight stacked in standard container without backlashes (for example, cotton wool, single-use medical clothes, latex gloves, free-flowing materials - food additives etc.). So, for example, the greatest possible productivity of installation with the accelerator 5.0 MeV, 15 kW will make about ton per hour at a dose 25 kGr and relation Dmax/Dmin=1.8. Very rough for energy range of electrons 2.5 - 7.5 MeV (and irrespective of type of the accelerator) productivity will change proportionally to power of the accelerator. It is necessary to note, that real productivity always less than the greatest possible because of factor of filling of

conveyor system which for different types of conveyors can makes about 0.7 - 0.9.

In case of processing the products having complex geometry, incorporating various materials (for example, syringes with needles, dialyzers, mitral valves, catheters etc.) theoretical calculation of productivity represents the big complexity. In this case in the best way productivity can be determined as a result of test irradiations.

ACCELERATORS ILU-TYPE FOR MEDICINE

The most perspective model of accelerators of ILU series for creation of complexes on sterilization is the accelerator to ILU-10.

On ILU accelerators established on test benches of our institute, active works for an improvement of various radiation technologies are spent in cooperation with the various organizations. So together with the Siberian Centre of Pharmacology and Biotechnologies, and also Institute of Cytology and Genetics works on immobilization of protolytic enzymes on polyethyleneoxide with the help ionizing radiation were carried out.

Low molecular weight Polyethylene glycols (PEG) are biologically inert substances that can be easily removed from the body. They are used in medicine as the carriers of various drugs. The PEO (PEG) gels are also used as the bases for cosmetic products.

The bacterial proteolytic enzymes decompose non-vital proteins and fibrin, and do not affect on vivid tissues, but they are unstable, allergogenic and pyrogenic. The radiation synthesis technology was successfully used for immobilization of proteolytic enzymes on polyethylene glycols. The preparations of the immobilized enzymes possess the prolonged lifetime, storage time and have the wide working range of temperature and pH of the medium.

A new medical preparation Trombovazim produced by radiation synthesis technology is the first preparation in the new line. Trombovazim has the wide spectrum of curing properties, first of all trombolytic and anti-inflammatory effects, and can be applied both enterally and parenterally. Trombovazim has already undergone clinical trials and widely used in clinical practice as enteral tombolytic agent.

Process of immobilization was realized using the electron accelerators type ILU-6 and ILU-10. The radiation synthesis technology was developed for pharmacological industry by corporation “SFM” (Novosibirsk, RF). Now this technology successfully uses in production of 7 original drugs for treatment of cardiovascular diseases and endocrine insufficiency.

REFERENCES

[1] V.L. Auslender. ILU-type electron accelerator for industrial technologies. Nuclear Instruments and Methods in Physical research, B 89 (1984), 46-48.

[2] V.L. Auslender, A.A. Bryzgin, L.A. Voronin, G.A. Vasiliev, V.A. Gorbunov, M. Korobeinikov, V.N. Kokin, S.A. Maximov, V.E. Nekhaev, A.D. Panfilov, V.M. Radchenko, V.O. .Tkachenko, A.A. Tuvik, B.L. Factrovich. ILU-type electron accelerators with energies higher than 5.0 MeV and power over 50 kW, Abstracts of Proceedings of XVII Workshop on accelerators of charged particles, Protvino, 2000.

[3] Auslender, R.A. Salimov. Electron accelerators of INP SB AS USSR for national economy, Atomnaja energija, v.44, issue 5, 1978. – pp. 403–408.

[4] V.L. Auslender et al. Electron Accelerator for Energy up to 5.0 MeV and Beam Power up to 50 kW with X-ray Converter, in XVIII Int. Workshop on Charged Particle Acc. Proc., Alushta, 2003.