POWER CONVERTERS FOR CELL ELECTROPORATION

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Abstract: This contribution refers about some topologies of power converters, which are used for medical purposes. The use of power converters in treatment of a cancer or an arrhythmia is a modern medical technique, which is still in development. The aim of the contribution is to compare current samples of power converters for medical purposes and briefly describe a design of a high-frequency power generator for AC electroporation.

Keywords: power supply, DC-DC converter, DC-AC converter, high frequency, MOSFET, IGBT

1 INTRODUCTION

A cell electroporation is a modern non-invasive method, which is suitable for treatment of some diseases. For example, the cancer and the arrhythmia. It is also used in genetic engineering, biotechnologies and food processing. Impacts on patient´s body are minimalized, so it leads to shortening the period of the treatment. The method requires rectangular high-voltage pulses with very short length. These pulses are generated by power converters, whose topologies are described in following statements. Two samples are from the USA and two have been developed at FEEC BUT.

2 CELL ELECTROPORATION

The cell electroporation is based on very short high-voltage pulses. These pulses are applicated to a treated tissue by special electrodes. Pulses lead to an increase of the permeability of the cell membrane. Ions, molecules and other chemical compounds can flow through nanopores created in the membrane. There are two ways of electroporation: reversible electroporation and irreversible electroporation. The difference between these two ways consists in a lifetime of nanopores. Temporary nanopores are created during reversible electroporation (RE), whereas irreversible electroporation (IRE) causes permanent nanopores, which lead to the death of the cell. The lifetime of nanopores depends on electrical properties of pulses (voltage, shape, frequency) and on biological properties of tissue and cells (dimensions, shape, density, temperature). Reversible electroporation is used in genetic engineering, irreversible electroporation is suitable for treatment of diseases. Electroporation can be also divided according to polarity of pulses: DC electroporation uses unipolar pulses and AC electroporation is based on bursts of high-frequency bipolar pulses. The length of the burst is similar to the length of one DC pulse. AC electroporation is suitable especially for the treatment of arrhythmia, because it does not cause muscular contractions [1].

3 TOPOLOGIES OF POWER CONVERTERS FOR CELL ELECTROPORATION

Power converters are usually divided into four groups: AC-DC (rectifiers), DC-DC (pulse converters), DC-AC (inverters) and AC-AC (triac regulators). These groups can be further classified according to different criteria. DC electroporation requires unipolar pulses, which are generated by DC-DC converters, whereas DC-AC inverters are suitable for high-frequency AC electroporation. Required output voltage reaches units of kilovolts with current about tens of amperes in both cases, so it is advantageous to use a pulse transformer to increase the voltage. The transformer also provides a galvanic isolation between AC mains and patient´s body. There are two different topologies, where the transformer is used. In the first case, the transformer is a part of the converter, which generates electroporating pulses. This topology is more advantageous, because there is not a risk of high-voltage pulse with uncontrollable length in the case of failure in the control or power circuits. One disadvantage can be seen in possible deformation of the pulse shape due to parasitic capacitance of the transformer. The second solution is a combination of DC-DC converter and high-voltage capacitors. These capacitors are charged from DC-DC converter with transformer. Electroporating pulses are generated by a high-voltage switch, which connects the capacitors with application electrodes. When the high-voltage switch fails, capacitors are discharged into the patient´s body. This the main disadvantage of this topology. On the other hand, high-voltage pulses are purely rectangular without any deformation. High-voltage supplies with capacitors must be equipped with safety transistor switches, which provide discharge of the capacitors. Some current high-voltage supplies are described in following paragraphs [2].

3.1 NANOKNIFE DEVICE FOR DC IRE

Nowadays, NanoKnife is the one and only commercial device, which is approved for DC electroporation. It is the topology with battery of high-voltage capacitors. A block diagram of this device is in Figure 1. The device is powered from AC mains. AC voltage is rectified by bridge rectifier with capacitor. The second stage is the DC-DC converter with pulse transformer, which charges the battery of high-voltage film capacitors. The output voltage of the converter can be regulated from 100 V to 3 kV. Electroporating pulses are generated by IGBT transistor. The device is equipped with 6 output terminals for 6 application electrodes, which are chosen by relay switch [3].

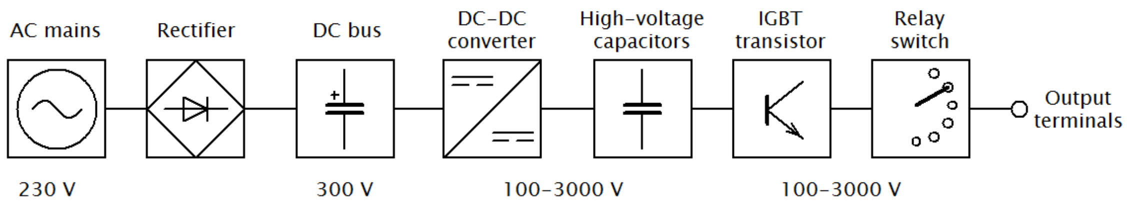

Figure 1: Block diagram of the NanoKnife device

The length of the pulse is variable from 20 to 100 µs. An operator can also adjust the count of the pulses from 10 to 100. Maximal value of the output current is 50 A. Pulses can by synchronized with EKG. The device contains safety circuit, which discharges high-voltage capacitors in the case of fault [3].

3.2 FEEC BUT HIGH-VOLTAGE SOURCE FOR DC IRE

This high-voltage source has been developed for experimental purposes, because NanoKnife device is very expensive. Block diagram of the source is in Figure 2 [1].

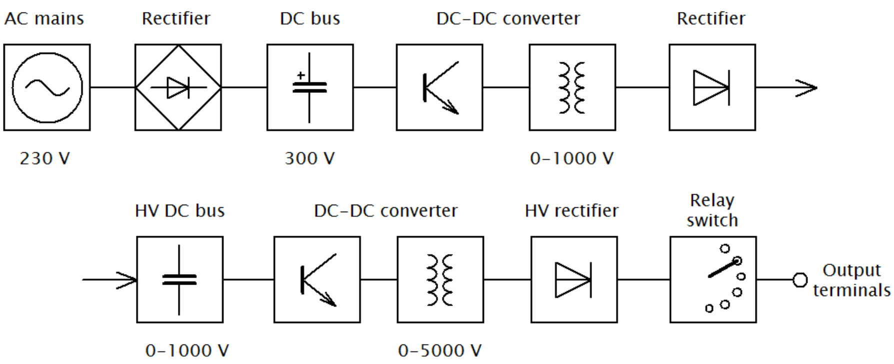

Figure 2: Block diagram of high-voltage source from FEEC BUT

It is a cascade of two DC-DC converters with pulse transformers. The first one is a two-switch forward converter, which is powered from AC mains. AC mains is rectified by bridge rectifier. The output voltage of this converter can be regulated from 0 to 1000 V. Output voltage is used for charging of the second DC bus, which is constructed from film capacitors. Total capacity of these capacitors is 110 µF. Electroporating pulses are generated by the second DC-DC converter. It is also the two-switch converter topology. The height of electroporating pulses can be set from 0 up to 5000 V. Maximal value of the output current is 100 A. These maximal values are higher than output parameters of NanoKnife device. Application electrodes are connected by relay switch. High-voltage pulses are rectified by HV rectifier created from 10 SiC diodes C4D20120D manufactured by CREE. Reverse voltage of each diode is 1200 V, so the total reverse voltage is 12 kV. The power part of the converter contains two IGBT modules FF1000R17IE4 by Infineon. Maximal collector to emitter voltage is 1700 V and maximal collector current is 1000 A. Modules are driven from integrated drivers 2ED300C17-S. Voltage and current are sensed by LEM sensors. The whole device is controlled by signal processor. Besides the height of the pulse, the operator is also able to adjust the pulse width from 20 to 150 µs and the time space between pulses from 0.2 to 2 s. Adjusted values are viewed on alphanumeric display [1].

3.3 HIGH-FREQUENCY GENERATOR FOR AC IRE

High-frequency generator for AC electroporation was patented in 2019, but commercial device is not available. The block scheme of the generator is in Figure 3.

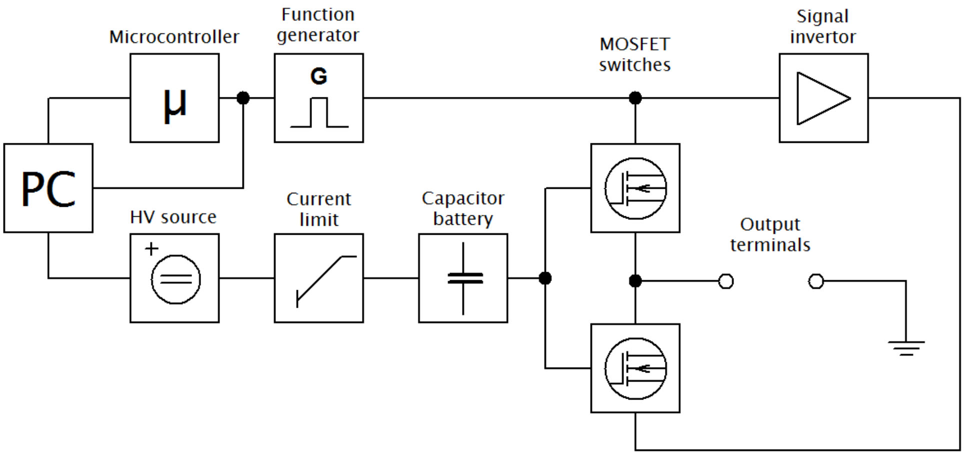

Figure 3: High-frequency generator for AC electroporation

A source of rectangular pulses is the function generator (Tektronix AFG 3011). The length of the burst, the space between bursts and the count of bursts is controlled by microcontroller (Arduino). Programmable laboratory supply LabSmith HVS448 works as a high-voltage source, which charges the battery of capacitors. Current limit is provided by resistors. Bursts of high-voltage pulses are generated by two MOSFET modules HV 1000 by DEI. The first module is driven from Tektronix generator directly, the second one through signal invertor (LM7171). Maximal input voltage of each module is 950 V and maximal output voltage is ± 850 V. Maximal output current into 50 Ω load is 17 A. A control part of each module is powered from AC mains. Output frequency can be varied from 250 kHz to 2 MHz, the length of each burst is 100 µs and the space between bursts is 1 s. Described high-frequency generator is created from connected laboratory appliances and does not contain pulse transformer. Application electrodes are connected directly to high-voltage capacitors by MOSFET switches. When the switch is damaged, capacitors are discharged into electroporated tissue [4].

4 FEEC BUT POWER CONVERTER FOR AC ELECTROPORATION

This converter was developed at FEEC BUT for experimental purposes. It is a compact device powered from AC mains. Two changeable pulse transformers allow to choose maximal output voltage value (2.5 kV or 1.3 kV). Maximal output current is 11 A (or 21 A with the second transformer), output peak power 27.5 kW is the same for both transformers. The operator can set the frequency of pulses from 65 to 470 kHz, the length of the burst from 40 to 120 µs and the space between following bursts from 0.5 to 1.5 s. Output values are adjusted by potentiometers. Output voltage value and the count of bursts is viewed on displays. Circuit diagram of the power part is in Figure 4 [2].

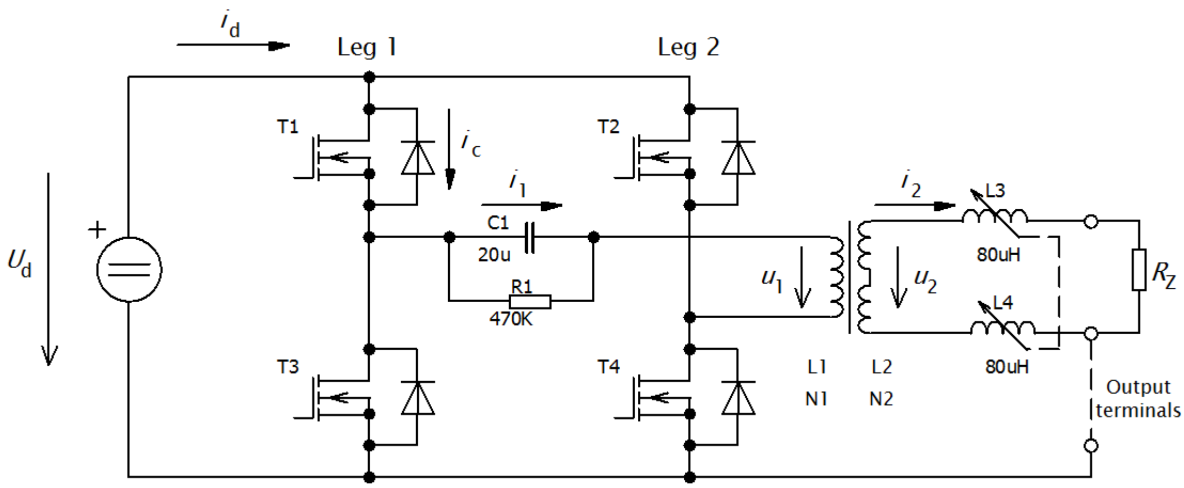

Figure 4: Circuit diagram of power part of the converter

Power part of DC-AC converter consists of four MOSFET transistors T_1-T_4. These transistors are switched in diagonals. It means that two transistors, T_1 and T_4 or T_2 and T_3 are switched together. Capacitor C_1 is used for elimination of DC magnetization of pulse transformer. Primary voltage u_1 and secondary voltage u_2 have rectangular shape and the height of secondary pulses is different with transfer ratio N_2/N_1 of the transformer. Primary current i_1 consists of magnetizing current i_μ and secondary current i_2 transferred to the primary winding. The shape of secondary current i_2 is rectangular and the shape of magnetizing current i_μ is triangular. The transformer is constructed on ferrite core Lj U 7020 CF 297. Ferrite material is used for its high resistivity, which eliminates eddy currents. The core does not contain air gap, which is useless here. Effective area of the core S_{Fe} is 400 mm^2, effective magnetic length l_{Fe} is 269.8 mm and relative magnetic permeability $\mu_{rFe} = 2100$. The number of primary turns N_1 is given by equation (1) and it is calculated for the lowest frequency $f = 65$ kHz:

$$N_1 = \frac{U_\mathrm{d}}{4 \cdot f \cdot B_\mathrm{max} \cdot S_\mathrm{Fe}} \tag{1}$$

Maximal flux density value B_max = 0.35 T is chosen. U_d is voltage in DC bus. For maximal value U_d = 320 V, the number of primary turns N_1 = 9 is obtained. This number is valid for both transformers. The number of secondary turns N_2 can be calculated from equation (2):

$$N_2 = \frac{U_2}{U_1} \cdot N_1 \tag{2}$$

U_1 is chosen voltage value in DC bus and U_2 are required maximal values of the output voltage. For U_1 = 300 V, N_1 = 9 and U_2 = 2500 V, N_2 = 75 is obtained. The second transformer with U_2 = 1300 V has N_2 = 39 secondary turns. Maximal drain current of transistors IXFK100N65X2 is 100 A. An over-current protection turns the driving circuits off, when primary current I_1max exceeds 96 A. Maximal value of magnetizing current Iμmax is given by equation (3):

$$I_\mathrm{\mu max} = \frac{B_\mathrm{max} \cdot l_\mathrm{Fe}}{N_1 \cdot \mu_0 \cdot \mu_\mathrm{rFe}} \tag{3}$$

For B_max = 0,35 T, l_Fe = 269.8 mm, N_1 = 9, $\mu_0 = 4 \cdot \pi \cdot 10^{-7}$ and μ_rFe = 2100, $I_\mathrm{\mu max}$ = 4 A is calculated. Maximal value of the output current I_2 can be calculated now (4):

$$I_2 = \frac{U_1 \cdot (I_\mathrm{1max} - I_\mathrm{\mu max})}{U_2} \tag{4}$$

For U_1 = 300 V, I_1max = 96 A, $I_\mathrm{\mu max}$ = 4 A and U_2 = 2500 V, I_2 = 11 A is obtained. When the second transformer with U_2 = 1300 V is mounted, secondary current reaches I_2 = 21 A. Magnetizing current decreases, when working frequency f rises. For that reason, maximal output current I_2 can exceed calculated values (4), when the operator sets higher working frequency. The cross-section area of the primary and secondary conductor must be divided into many thin insulated conductors because of skin effect. Variable inductors L_3 and L_4 (Figure 4) are used for elimination of high-frequency capacitive currents, which flow through the parasitic capacity of the transformer into patient´s body and then into the ground. These currents can affect measuring devices [2].

5 CONCLUSION

This contribution was focused on power converters used for medical purposes, especially for cell electroporation. DC electroporation uses unipolar pulses, that can be generated by DC-DC converters. AC electroporation is based on bursts of high-frequency bipolar pulses, which can be generated by DC-AC converters. In topologies with pulse transformers, electroporating pulses are transmitted by the transformer, which provides the galvanic isolation of patient´s body from AC mains. Different topologies are based on high-voltage capacitors, which are connected to application electrodes by solid-state switches with MOSFET or IGBT transistors. Both topologies have their advantages and disadvantages, that are mentioned in relevant paragraphs. Two described converters are from the USA and two have been designed and developed at FEEC BUT.

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