Glioblastoma multiforme (GBM) is considered the most aggressive and lethal form of brain tumour due to high degree of tumour cell infiltration into surrounding brain tissue. The current standard of care for newly diagnosed GBM is maximal safe surgical resection followed by the administration of temozolomide (TMZ) alongside external beam radiation. Although chemoradiotherapy improved median survival from 12.1 to 14.6 months when compared with radiation alone, the survival advantages are only palliative. Glioblastoma, even when totally resected, recurs due to its infiltrative nature. Most of recurrences ale local, within 2 cm of the primary tumour. So, the most significant approach to treat glioblastoma possesses local drug delivery systems. This kind of dosage form will have importance only if they provide sustained release for at least a few weeks with no systemic leakage.

This project aims to optimize the multi-drug delivery system in a form of the nonwoven wafer for controlled release of anticancer drug, autophagy inhibitor and radiosensitizer, as a proposal of the future treatment of glioblastoma that will be combined with radiation.

Designed DDS will be composed of bioresorbable polymers and obtained with the use of electrospinning technique. When compared to other dosage forms electrospun nonwoven can reduce the toxicity and increase the local drug concentration. The prolonged but delayed release of the drugs will be optimized to correlate the start of chemotherapy with radiation by application of core-shell fibres as well as mixed fibres (like cable wire) but also the appropriate order of the nonwoven layers. The studied polymers will be obtained with the use of L-lactide, glycolide, ε-caprolactone and trimethylene carbonate. After sterilization and detailed analyses of physicochemical properties, sandwich-like nonwovens will be subjected to hydrolytic degradation. The nonwoven DDSs will be tested by means of the nuclear magnetic resonance spectroscopy, gel permeation chromatography, differential scanning calorimetry, Fourier transform infrared spectroscopy and scanning electron microscopy. Amount of released drugs will be evaluated with the use of high-pressure liquid chromatography. The effectiveness of the proposed multi-drug delivery system will be tested in human and murine glioma cell cultures as well as on animals.

Results of this project will help to understand the kinetics and mechanisms of drugs' release from bioresorbable nonwoven, that are in turn associated with degradation mechanism of a polymer vehicle, but also permit the prediction and the adjustment of delivered doses of the drugs. The influence of drugs on hydrolytic degradation and release kinetics but also the impact of sterilization on prepared DDSs will be studied. *In vitro* tests on cell cultures and *in vivo* tests on an animal model will allow to verify the effectiveness of the proposed electrospun nonwoven in combination with radiotherapy. Without this knowledge, there is no possibility to develop new drug dosage form. It is believed that obtained multilayer nonwoven as DDS show significant promise for future translation into substantial gains in GBM patient outcomes.