During radiotherapy treatment of brain tumours, some of the normal, non-tumour brain tissue is unavoidably irradiated. This can affect how the brain functions, such as memory loss and inability to process new information, impacting the quality of life of surviving patients. This dissertation aims to understand the mechanisms behind this brain decline, focusing on the brain regions most affected by radiotherapy and microglia, the main immune cells of the brain. Another aim is to elucidate the role of advanced radiotherapy technologies, such as proton therapy. To study the effect of radiotherapy and proton therapy on the normal brain, we used rodent models and human post-mortem brain tissues. We discovered that brain irradiation increases the immune response of microglia to future inflammatory insults. We also found that the effect of proton therapy and conventional radiotherapy on microglia is similar and that this response is limited to the irradiated parts of the brain. To fully benefit from the advantages of proton therapy, it is important to know how different brain regions respond to radiation. We reviewed this regional variation in a literature study for several organs. We also further studied this response in rodents that received radiation in specific parts of the brains and measured brain function using behavioural tests. Lastly, to better understand the effects of radiotherapy on the human brain, we analysed the post-mortem brain tissue of glioblastoma patients. Our research indicates that glioblastoma and its treatment accelerate the ageing process of the brain, inducing changes similar to Alzheimer's disease.