SUMMARY

Nanoparticles (NPs) have considerable potential in targeted medicine. NPs can merge various functions and serve as labels for imaging or as nanocarriers in therapy. Modification of NPs with targeting ligands can lead to highly specific interactions with targeted cancer cells. However, the efficacy of targeting depends on the ratio between specific and non-specific interactions of a NP with the cell. Non-specific interactions of NPs are unrelated to targeted receptors and need to be eliminated in order to decrease background noise during imaging and adverse effect of drugs on healthy tissues.

In this thesis, surface modifications of NPs were explored mainly on biocompatible carbon NPs called nanodiamonds (NDs), which have exceptional fluorescent properties such as long fluorescence lifetime, no photobleaching and photoblinking and sensitivity of their fluorescence to electric and magnetic field. Main issues addressed in this thesis are low colloidal stability of NDs in buffers and media, their non-specific interactions with proteins and cells and limited approaches for ND surface modifications. These issues were solved by coating NDs with a layer of biocompatible, hydrophilic, and electroneutral poly(ethylene glycol) or poly[*N*-(2-hydroxypropyl) methacrylamide] polymers. Optimized polymer coating provided NDs steric stabilization in concentrated buffers, eliminated non-specific interactions with cells and enabled further bioorthogonal functionalization of NDs. Modification of NDs was demonstrated using various targeting ligands. First, NDs were modified with targeting peptide cyclic RGD. These conjugates showed reasonable targeting effect thanks to the elimination of non-specific interactions. The specific interactions of NDs with cancer cells were further improved upon surface modification with transferrin and small-molecule inhibitor of glutamate carboxypeptidase II.

The developed biocompatible interface of NDs enabled further biomedical applications. First, NDs with gold layer and polymer coating were shown to efficiently target and kill cancer cells using photothermal ablation. Second, optical relaxometric nanosensors working under physiological conditions were created from NDs with polymer layer containing Gd^{3+}complexes. The chemically programmable structure of the polymer enabled optical readout of localized chemical processes occurring on an extremely small scale (10^{-22}–10^{-20} mol).