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Local delivery of poly lactic-co-glycolic acid microspheres containing imatinib mesylate inhibits intracranial xenograft glioma growth.

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PURPOSE: In an effort to develop new therapeutic strategies to treat malignant gliomas, we have designed poly (lactic-co-glycolic) acid (PLGA) microparticles that deliver imatinib mesylate, a small molecule tyrosine kinase inhibitor. The local continuous release of imatinib mesylate at the tumor site overcomes many obstacles associated with systemic delivery.

EXPERIMENTAL DESIGN: Polymeric microspheres were prepared from various compositions of PLGA and loaded with imatinib mesylate. Imatinib release profiles, biological activity, and effect on PDGFR-B phosphorylation were confirmed in vitro. The therapeutic efficacy of imatinib microspheres was examined in two s.c. and orthotopic human glioblastoma xenograft models. **RESULTS:** A single local injection of PLGA microspheres loaded with a low concentration of imatinib mesylate led to 88% and 79% reduction in s.c. human (U87-MG) and murine (GL261) glioma tumors, respectively. PLGA-imatinib mesylate administered intracranially led to a 79% reduction in U87MG tumor volume.

Immunohistochemical analysis showed a marked decrease in proliferation indices and tumor vessel density in the s.c. model and induction of apoptosis in an intracranial model.

CONCLUSION: This is the first study to show the therapeutic efficacy of the local delivery of imatinib mesylate using a polymeric delivery system.

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