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ABSTRACT
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Differential Radiosensitizing Potential of Temozolomide in MGMT Promoter Methylated Glioblastoma Multiforme Cell Lines

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Purpose
To investigate the radiosensitizing potential of temozolomide (TMZ) for human glioblastoma multiforme (GBM) cell lines using single-dose and fractionated γ-irradiation.

Methods and Materials
Three genetically characterized human GBM cell lines (AMC-3046, VU-109, and VU-122) were exposed to various single (0–6 Gy) and daily fractionated doses (2 Gy per fraction) of γ-irradiation. Repeated TMZ doses were given before and concurrent with irradiation treatment. Immediately plated clonogenic cell-survival curves were determined for both the single-dose and the fractionated irradiation experiments. To establish the net effect of clonogenic cell survival and cell proliferation, growth curves were determined, expressed as the number of surviving cells.

Results
All three cell lines showed MGMT promoter methylation, lacked MGMT protein expression, and were sensitive to TMZ. The isotoxic TMZ concentrations used were in a clinically feasible range of 10 μmol/L (AMC-3046), 3 μmol/L (VU-109), and 2.5 μmol/L (VU-122). Temozolomide was able to radiosensitize two cell lines (AMC 3046 and VU-122) using single-dose irradiation. A reduction in the number of surviving cells after treatment with the combination of TMZ and fractionated irradiation was seen in all three cell lines, but only AMC 3046 showed a radiosensitizing effect.

Conclusions
This study on TMZ-sensitive GBM cell lines shows that TMZ can act as a radiosensitizer and is at least additive to γ-irradiation. Enhancement of the radiation response by TMZ seems to be independent of the epigenetically silenced MGMT gene.

Human GBM cell lines, Temozolomide, MGMT, Radiosensitization, Fractionated irradiation

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