How to build a predictive model of treatment outcome in perioperative high dose-rate brachytherapy (PHDRB).

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Introduction

This study aims to generate a clinical predictive model of locoregional failure after: 1. complete surgical resection, 2. perioperative high dose rate brachytherapy (PHDRB) and 3. external beam radiation therapy (EBRT).

PHDRB
• added advantages: CT planning, dose optimisation and radiation protection.
• ideally suited in patients at higher risk of locoregional failure (due to limitations of the surgery or tumor characteristics.
• delivers higher doses of radiation over a well delineated area of the surgical bed that has the highest probability of containing residual tumor cells

Several parameters will be analysed to identify independent predictors of locoregional failure, that will be used to stratify patients into groups of different locoregional failure risk

Materials and methods

186 patients: Head and neck cancer, sarcomas, gynecological and colorectal cancer and other cancers.

Treatment protocol:

Surgery
• Complete resection of the tumor

PHDRB
• Negative margins ≥ 10 mm: 16 Gy (4 b.i.d.)
• Negative <10 mm or Positive margins: 24 Gy (6 b.i.d.)
• 45 Gy in 25 daily treatments four weeks later
• Concurrent chemotherapy for each disease situation

PHDRB technique:

Statistical analysis:

Univariate analysis
Effect on locoregional control of several parameters

Potential factors
Treatment-related factors

Multivariate analysis
Cox Proportional Hazards Model

Generation of the predictive model
Validated in a ROC model

Results

Positive and negative <1mm surgical margins:
3.4-fold higher risk of locoregional failure

Tumors larger than 3 cm:
1.9-fold greater risk of locoregional failure

Variables used to generate the predictive model:
1. Surgical margins (M5KCC definition)
2. Tumor size

Discussion

Tumor size and surgical margins:
• proportional to the number of clonogens remaining after surgery
• predictive of locoregional failure

Other factors usually associated with an aggressive clinical behaviour were not statistically significant in this study (tumor site or status)

The risk of locoregional failure depends on the number of residual clonogens rather than on tumor type or status.

This predictive model can be applied to a wide range of clinical settings where postoperative irradiation is necessary

Debate: routine use of PHDRB in large tumors

Patients in the high risk and very high risk categories may require dose escalation

Despite the statistical significance of the present predictive model, it is not highly predictive (AUC=0.72). Hence, more research is needed to increase the predictive ability of the model.

Conclusions

• Surgical margins and tumor size determine long-term locoregional status in a variety of common human cancers.
• Locoregional outcome is mainly dependent on the number of tumor clonogens remaining after surgery and does not seem to be strongly related to other tumor factors

Literature cited

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