

Thermoradiochemotherapy: Trimodality Cancer Treatment

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Introduction

To overcome on tumor cells and having better clinical results, there is an attention to apply combination of treatment regimens. The reasons for combination therapy is to reduce problems exist after radiotherapy (RT) with χ and/or γ rays. One of the most important problems is hypoxic cells in the centre of tumors. Due to insufficient blood perfusion, these cells are more resistant to RT. The oxygen enhancement ratio for χ and γ rays is 2-3. Thus, to reach the same cell damages in hypoxic conditions, one needs to increase radiation dose 2-3 times; that certainly will increase the absorbed dose in normal tissues. During the recent decades, using drugs (those that specifically increase sensitivity of the hypoxic cells) and hyperthermia (HT) [the controlled increased of the tumor temperature by 3-8°C for 60-90 min] are considered to surmount the hypoxic cells; as they remarkably increase radio- and chemo sensitivity of the hypoxic cells. The purpose of this letter is to provide an overview on the application of HT in adjuvant with conventional cancer treatment modalities; i.e., RT and chemotherapy (ChT).

Tumor masses tend to have hypoxic cells within the inner part of the tumor. Cells in hypoxic areas are relatively radio-resistant, but very sensitive to HT and ChT availability will be less in insufficiently perfused areas. HT is especially effective in cells under conditions of hypoxia and low pH. HT damages the membranes, cytoskeleton, and nucleus functions of malignant cells. It causes irreversible damage to cellular perspiration of these cells. HT above 41°C also pushes cancer cells toward acidosis (reduction cellular pH), which decreases the cells' viability and transplantability. Furthermore, HT preferentially kills cells in the S-phase of the cell cycle, which are known to be resistant to RT. It is also thought that HT induced accumulation of proteins inhibits the malignant cells from repairing the damage sustained. Tumor blood flow is increased by HT despite the fact that tumor-formed vessels do not expand in response to heat. This makes HT an ideal complementary treatment to both RT and ChT. The HT mechanisms and its effect on tumor cells justify using additive complementary of HT and RT, in which during period of RT, 5-6 sessions of HT is applied once weekly. A number of well-controlled, randomized trials comparing RT plus HT with RT alone demonstrate that the average complete response for RT alone can be increased significantly by the addition of HT. Moreover, for the combination of ChT and HT, special cooperation can explain the additive effects. Drug concentration will be less in the insufficiently perfused tumor regions. Furthermore, many drugs are potentiated by HT. It has been shown for the drugs that the addition of HT to ChT can counteract drug resistance. The most important mechanisms for an interactive effect are increasing intracellular drug uptake, enhanced DNA damage, and higher intra-tumor drug concentrations; resulting from an increase in the blood flow. The effect of the drug can be enhanced by a factor of 1.2-10. Whether the clinical combination of HT and ChT leads to therapeutic gain depends on the temperature increase in the organs for which the used drug is toxic and the heating method [1].

Nowadays, there is an increasing interest in the clinical application of triple modality treatment, in which RT, ChT and HT are combined. Japanese were probably the first to test tri-modality treatment, and they

have demonstrated the value of adding HT in patients with esophageal cancer. Most of the recent studies on preoperative treatment in rectal cancer, head and neck tumors, and recurrent breast cancer have made it clear that tri-modality treatment is feasible and appears effective [2].

Majority of the clinical trial studies up to 2015 show a statistical significant higher (up to a doubling) tumor control and/or cure rate for the combined treatment modality. Additionally, all studies report comparable acute and late toxicity. The positive results of the most recent trials explain the renewed enthusiasm in HT, which is reflected in the growing number of institutes interested in the application of HT [3].

In the past, when intra-lumen and/or intra-tumor thermometer(s) was used, the most important limitation in HT application was thermometry. Fortunately, using advanced equipment for quality control has solved most of the problems [4]. Nowadays, the MR-thermometry, which is a 3D and non-invasive method applying hybrid system of magnetic resonance imaging (MRI) accompanying with HT applicator, can characterize temperature as well as perfusion [5].

In conclusion, regional HT combined with RT, ChT or both have shown impressive results in local advanced tumors of certain entities in terms of objective response rate, local tumor control, palliative effects, and survival rate, without increasing toxicity; in different tumor sites such as breast cancer, melanoma, head and neck, cervix cancer and glioblastoma. HT is probably the most potent radio- and chemo- sensitizer known to date. However, it is not yet a fully developed modality for all tumor sites. There are still problems with the routine clinical application of HT, and there is still room for further technological improvements.

References

1. Hildebrandt B, Wust P (2007) The biologic rationale of hyperthermia. *Cancer Treat Res* 134:171-184.
2. Westermann AM, Jones EL, Schem BC, van der Steen-Banasik EM, Koper P, et al. (2005) First results of triple modality treatment by combining radiotherapy, chemotherapy and hyperthermia for treatment of stage IIB-III-IVA cervical cancer. *Cancer* 104: 763-770.
3. Datta NR, Ordóñez SG, Gaipal US, Paulides MM, Crezee H, et al. (2015) Local hyperthermia combined with radiotherapy and/or chemotherapy: Recent advances and promises for the future. *Cancer Treat Rev* 41:742-753.
4. Fatehi D, van Rhoon GC (2008) SAR-characteristics of the Sigma-60-Ellipse applicator. *Int J of Hyperthermia* 24: 347-356.
5. Fatehi D, van Rhoon CG, van der Zee J (2009) Thermo radiotherapy of cancer: An effective approach. *Australasian Medical Journal* 1: 224-234.

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