Table 1. Mechanisms of action of hyperthermia.

|  |  |  |  |
| --- | --- | --- | --- |
|  | 39-41 | 41- 43 | 43-45 |
| Direct Citotoxic Effects | Slight growth arrest | Reversible growth arrest   * Mainly in phase M & S * Brief RNA synthesis impaired * Prolonged DNA synthesis impaired | Irreversible growth arrest   * Permanent protein denaturalization * DNA repair impaired * Activation of both ways of apoptosis |
| Immune effects | Initial increase intracelular HSP followed by increase of extracelular HSP   * Signals to inmune cells * Cross-priming of CD8+Tcells * Dendritic cell activation * Natural Killer activation * Increase citocine realease (Il-6, IL-10) | As above | Altered citocine production  Inactivation of inmune cells  Reduced expresion of extracelular HSP |
| Vascular effects | Vasodilatation which means:  Improved tumour blood flow   * Improve tisular O2 * Reduce acidosis * Improve drug absortion | Improved tumor blood flow:   * Improve tumor oxygenation * Improve drug delivery | Reduced tumour blood flow due to vascular colapse   * Microthrombosis * Endothelial cell damage * Vessel permeation * Increased acidosis and reduce tisular O2 |

Adapted from Rampersaud et al [11](#_ENREF_11)

Table 2. Characteristic of Devices for Intravesical CHT Treatment

|  |  |  |  |
| --- | --- | --- | --- |
| Device | SynergoTM | BWT systemTM | CombatTM |
| Heat Source | Intravesical 915 MHz microwave antenna  *(Recirculating cooling system)* | External heating plates  *(Recirculating heating system)* | External flat, low volume heat exchanger  *(Recirculating heating system)* |
| Temperature & fluctuation | 40-44°C +/- 3°C | 45 °C+/ ? | 43.5 °C+/-1°C |
| Priming volumen | +/- 100 mL | +/- 50 mL | +/- 30 mL |
| Catheter characteristics | 20 Fr. Rigid  (Radiofrequency emisor + cooling system inside) | 18 Fr Flexible | 16 Fr Flexible |
| Advantages | Strong supporting evidence *(neoadjuvant & adjuvant)*  Long term follow up  Proved superior to BCG  Proved effectivenes against CIS | Simple and Cheap | Lower dilution of MMC  Proved effectiveness in sequential schedules  Proved neoadjuvant effectiveness  Medium term follow up  Simple and Cheap |
| Disadvantages | Higher side effects  Lower patient tolerance  Intravesical Hot and cold spots  Expensive device and disposables  Continuous machine control requiered while working | Limited evidence  Quick & Turbulent flow + higher temperature *(increase hematuria and reduce patient tolerance)* | Limited evidence (*multicentric studies ongoing*) |