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 productionInactivation 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 upProved superior to BCGProved effectivenes against CIS | Simple and Cheap | Lower dilution of MMCProved effectiveness in sequential schedulesProved neoadjuvant effectivenessMedium term follow upSimple and Cheap |
| Disadvantages | Higher side effects Lower patient toleranceIntravesical Hot and cold spotsExpensive device and disposablesContinuous machine control requiered while working | Limited evidenceQuick & Turbulent flow + higher temperature *(increase hematuria and reduce patient tolerance)* | Limited evidence (*multicentric studies ongoing*) |