New modality of curietherapy with holmium oxide submicronic particles

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INTRODUCTION

The main advantage of using radioactive sub-micro/nanoparticles as curietherapy agent is the possibility to obtain a more homogeneous and intense radio effect and consequently improve the anti-tumoral effect and decrease the probability of relapse.

The aim of this study is to demonstrate that sub-micronic Nano holmium oxide particles (NanoH™) can be activated without alteration of the particle structure and that can be directly injected in a tumour with high intra-tumoral remanence, without overall adverse effect, and with evident anti-tumoral effect.

BRACHOTHERAPY : STAT OF ART & DEVELOPPEMENT

Brachtherapy

- Radioactive source piece inside or next to the area requiring treatment
- Decreased radiation after being associated with cysteine angiography
- Sealed source radiotherapy or endomicrotherapy

Advantage of particles in brachtherapy

- Noninvasive insertion (injectable)
- Better intra-tumoral dispersal
- Intra-tumoral persistence
- Elimination of the diffused particles
- Side effects
- Problem of radio-protection

Advantage of Holmium

- Very high lanthanide content
- Very high specific radioactivity

Lanthanide oxide VS Lanthanide

Type of nanoparticles

<table>
<thead>
<tr>
<th>Type of nanoparticles</th>
<th>Gd/kg</th>
<th>C/kg</th>
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<tbody>
<tr>
<td>Gd2O3 PLa nanoparticles (72% w/w)</td>
<td>33</td>
<td>0.99</td>
</tr>
<tr>
<td>No PLA nanoparticles (20% w/w)</td>
<td>37</td>
<td>1.00</td>
</tr>
<tr>
<td>No oxide nanoparticles (no content 40%)</td>
<td>150</td>
<td>3.52</td>
</tr>
</tbody>
</table>

Present Study

Sub-micro/Nano-Particles VS Microparticles

- Injectable by a hypodermic syringe
- Injectable by various ways (IV, IA, intra-peritoneal and intra-tumoral way
- Better intra-tumoral dispersal (nano/objet)

Injection of the Holmium Oxide sub-micro/Nano Particles

After the suspension of micro-particles, they are injectable by TMT and/or syringes

High pressure injection

- TMT : The Targeted Multi Therapy is based on the high pressure injection of any kind of active agent (steam, chemical agents, radioactive agents) by using a perfused needle/microtube inserted/implanted inside the tumour (CERMA™) The injection technique is already CE method and on the market regarding injection of overheated steam for vessel disorders.

Intra-tumoral remanence studies

Ex vivo vivaluation

- Kuv : 1st injection of the right axel of a suspension of holmium/calcium particles (5% w/v with 106 particles/cm3)
- Ex vivo measurement of the right axel of a suspension of holmium/calcium particles (5% w/v with 106 particles/cm3)
- Ex vivo measurement of the right axel of a suspension of holmium/calcium particles (5% w/v with 106 particles/cm3)

Therapeutic Test

- We tested therapeutic efficiency of 800 mCi Holmium oxide particles (NanoH) in 10 rats (10 tumors, 3 groups: NanoH (26 tumors), saline (26 tumors), no treatment (26 tumors)). In addition, 3 rats were activated on the left axel particles in NanoH petrol. In suspension in saline TMT (100% activity) 50% of tumors were destroyed.
- Therapeutic effect and side effect were evaluated in a 4 weeks cycle.
- The average growth inhibition values between 07F and 011 was 10% for saline and 40% for NanoH.

CONCLUSION

The proposed brachtherapy methodology (particles synthesis, activation, injection, SPECT and MRI analysis, biodistribution, therapeutic effect) based on the use of submicronic neutron-activated holmium oxide particles has been successfully validated. It is a promising new method for curietherapy by direct intra-tumoral injection, with perspectives of additional treatment in glioblastoma (by intra-tumoral injection), in peritoneal or pleural carcinoma (intra-cavity injection) or hepatocarcinoma (intra-arterial injection).