ESRF	**Experiment title:** Real time and quantification of contrast agent (Iodine / Gadolinium) concentration after convection enhanced delivery into an agarose gel phantom	**Experiment number**: 21162
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Report

Malignant brain tumors are still associated with a poor prognosis despite advances in neurosurgery, radiotherapy and chemotherapy. State-of-the-art treatment for patients with a glioblastome multiforme (GBM) median survival is only about 12 to 15 months. New approaches to improve the high grade glioma treatment need to be developed and optimized. One way consists to combine the injection of a high-Z element (iodine, gadolinium) or a chemotherapeutic agent (usually platinated drugs) in combination with X-irradiation. These injections are critical for the treatment process because it has to target all the tumor tissue and preserve the healthy one. However, the presence of the blood brain barrier, that is a natural regulator in normal conditions, hampers the distribution of drugs for treating brain tumors. Intracerebral injections into the tumors bypass the BBB, provide higher drug concentration in the tumoral bed than systemic injections, and lead to lower systemic toxicity. Convection-Enhanced Delivery (CED), have been proposed by Bobo *et al.* 1994[1] as a refinement of this method of injection. It consists of a direct injection into the brain tumor with low and controlled flow rate of infusion. This method allows obtaining higher volumes of distribution containing high concentrations levels in the target tissue. Imaging studies at low spatial resolution have been performed on both cerebral tumor-bearing and healthy rats at the ID17 Medical Beamline to measure the distribution of iodine in the brain tissue (Rousseau *et al.* 2007[2]). This study has shown that distributions are highly dependent of the type of tissue (healthy/tumor) and also infusion parameters. Reflux that can occur along the catheter path can lead to drug injection into adjacent non-targeted brain structures also depend on these parameters, as previously reported by Morisson *et al*. 1994[3]. Homogeneous and isotropic gels (low-concentrated agarose) have been developed as an experimental model of brain tissue that reproduce some of its properties (Chen *et al.* 2004[4]). These inert gels are a reproducible model that simplify relationships infusion parameters and experimentally observed agent distributions, while reducing the animal use. Standard imaging modalities for observing such *in situ* distributions non invasively are *e.g.* visible transmission

videomicroscopy with relative dye concentration measurements and Magnetic Resonance Imaging (Chen *et al.* 2004[4], Chen *et al.* 2007[5]). Here, we studied CED distributions of an iodinated contrast agent in gels by monitoring during infusion the spread of the tracer with high resolution imaging. This methodology was applied to several infusion procedures. Thanks to a reduced acquisition time, we could image every three minutes the spread of the agent through the gel porous media, limiting motion artifacts. These data have indicated a stronger temporal dynamic at short times after beginning of infusion that we could correlate with analytical models of flow through porous media. Further investigations to improve our understanding of these hydrodynamic and transport mecanisms in porous media are still needed and are under the scope of coming studies.

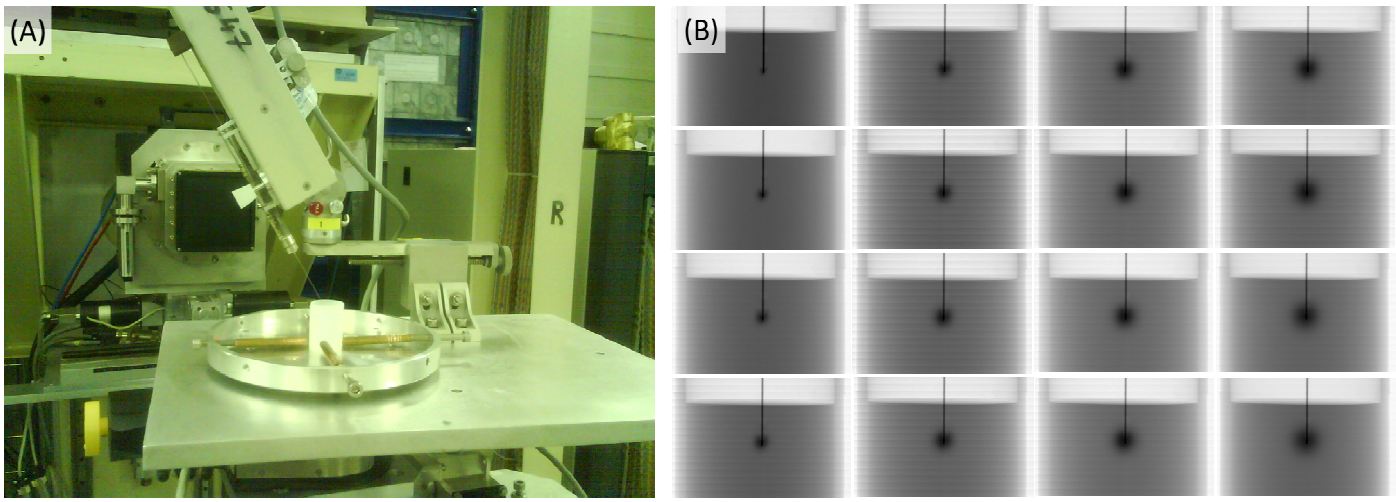

Figure 1 : (A) Picture of the experimental setup. (B) Radiographic images of a gel during a 40 minute infusion of 20 µL of an iodine contrast agent, taken every three minutes (from 2 to 49 min ; reading from top to bottom, and from left to right).

References

(1) Bobo RH, L. D., Akbasak A, Morrison PF, Dedrick RL, Oldfield EH *Proceedings Of The National Academy Of Sciences Of The United States Of America* 1994, *91*, 2076-2080.
(2) Rousseau J, B. C., Esteve F, Elleaume H *International Journal Of Radiation Oncology Biology Physics* 2007, *68*, 943-951.
(3) Morrison PF, L. D., Bobo H, Oldfield EH, Dedrick RL *American Journal Of Physiology* 1994, *266*, R292-R305.
(4) Chen ZJ, G. G., Broaddus WC, Prabhu SS, Fillmore H, Mitchell RM, Corwin FD, Fatouros PP *Journal Of Neurosurgery* 2004, *101*, 314-322.
(5) Chen XM, A. G., Mareci TH, Sarntinoranont M In *29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*: Lyon, FRANCE, 2007; Vol. VOLS 1-16; pp 2887-2890.