Observing IUDs “in-situ”

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Copper-bearing intrauterine devices (CuIUDs) are frequently used for long-acting reversible contraception. The release of copper ions into the fluid medium of the uterus reduces the probability of ovum fertilisation and endometrial adhesion. It is widely believed that the primary source of these ions is cuprite (Cu_2O) formed on the device surface through in-utero corrosion. However, cuprite has a very low solubility at the pH and temperature of the uterine fluid so this seems unlikely, especially when far more soluble compounds such as copper sulphate and chloride may also be formed.

Further development of the CuIUD involves exploiting geometries with a high surface area to volume ratio compared to the traditional “coil” combined with enhanced copper dissolution, e.g. through exploiting galvanic corrosion. However, the interactions between the copper and the uterine fluid need to be better understood.

We studied the surface reaction products *in-situ* using XRD* on XMaS **[1]** with a custom made portable electrochemical cell (peCell), filled with simulated uterine fluid (**Fig. 16**). Copper coupons with three levels of partial gold coating (1.4%, 5% and 25% by area) were studied simultaneously to assess the influence of galvanic corrosion. Our approach is intended to eliminate misleading results from *in-utero* samples subjected to removal, cleaning and storage prior to analysis. This may cause insoluble crusts to be formed. The new peCell allowed us to follow the surface changes over 8 consecutive days. However, as it is both portable and designed to maintain conditions indefinitely, longer term experiments are possible in the future.

Over a period of 8 days, copper with less than 25% coverage of gold became coated with Cu_2O and released colloidal Cu_2S into the fluid. Neither of these compounds is likely to promote anticonception as they are both insoluble at the uterine pH and temperature. Crystalline NaCl was also deposited from the fluid. The surfaces and the fluid became visibly blackened.

Surface CuCl and CuS (both insoluble) were also observed for the lowest gold coverage. (CuCl reacts with water to form Cu_2O and with water vapour in the air to form $Cu_2(OH)_3Cl$ and so can distort the results from rinsed and stored samples analysed *ex-situ*). The sample with 25% gold coverage showed little formation of insoluble products although CuO and CuS were present. However, a crystalline phase of $CuCl_2$ became visible to XRD after around 7 days. This is extremely soluble under *in-vivo* conditions and the fact that it was observed as a solid indicates a high rate of production at the surface. The XRD will not see products which are in solution, but the release of Cu++ ions likely takes place through reaction with chlorine naturally present in uterine fluid and in our simulant, as indicated by the results from the highest gold coverage.

Partial gold coating strongly modifies the behaviour of the copper in the simulated uterine environment in an area dependent way and, for sufficiently large areas, appears to drive the reactions to form more soluble compounds therefore putting more copper in solution. Longer term experiments using synchrotron XRD of the surface and XAS* of the fluid will be carried out to verify and extend these results with the objective of further improving frameless intrauterine devices.

[1] R.A. Grayburn *et al.*, Bioelectrochemistry 110, 41 (2016).

* See glossary p.5 for definition.

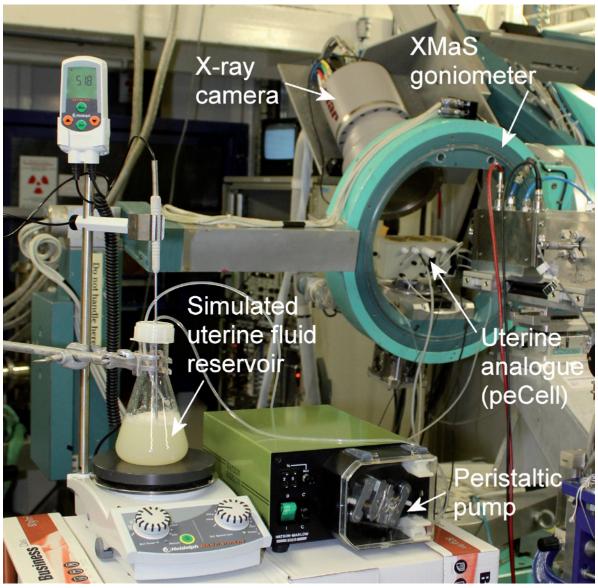

Fig. 16: *Portable electrochemical/environmental cell (peCell) containing copper coupons part-coated with gold in circulating simulated uterine fluid.*