JPAC 13-65

Joint UKBTS Professional Advisory Committee [1]
Summary Sheet

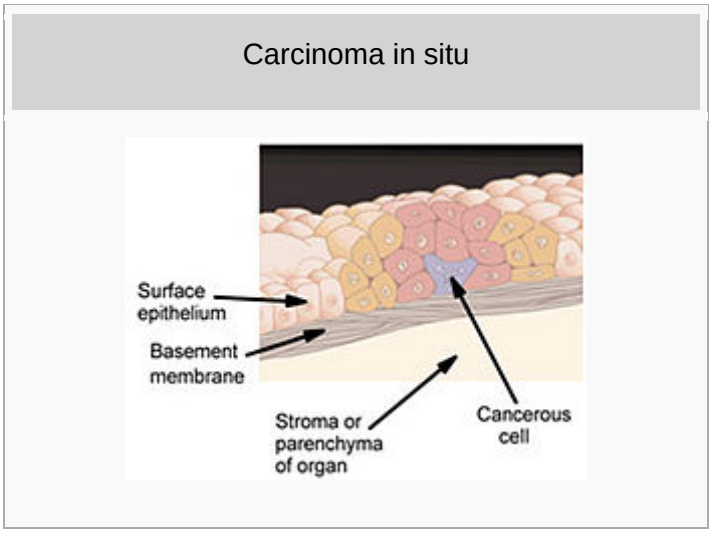
1. Paper for the JPAC meeting on:	14 November 2013
2. Date submitted:	31 October 2013
3. Title (including version no.):	Carcinoma in Situ
4. Author(s):	Dr Sue Barnes, Chair of the SAC on Care and Selection of Donors
5. Brief summary:	The DSG allows the acceptance of a very limited number of donors diagnosed, treated and cured and only non-clonal premalignant disease. BSQR 2005 allows acceptance of donors with 'in situ cancer with complete recovery'. The WHO recommends acceptance if 'in situ carcinoma (e.g. BCC) has been successfully treated. The CoE recommends the donor may be accepted immediately after successful removal and cure. We are thus recommending a change to the current DSG entry for Malignancy to allow a wider range of carcinomas in situ to be accepted once cured and to clarify the position re premalignant conditions.
6. Action required by the JPAC: (What do you want JPAC to do in response to this paper?) e.g. • endorse a specific recommendation • advise where there is a choice of possible actions • advise on priorities within the work plan • provide a steer on policy	Discuss and approve recommendation
7. Any other relevant information:	

[1] **Joint U**nited **K**ingdom **B**lood **T**ransfusion **S**ervices **Professional Advisory Committee**

Carcinoma in situ

Background

Carcinoma *in situ* (CIS) is an early form of cancer that is defined by the absence of invasion of tumor cells into the surrounding tissue, usually before penetration through the basement membrane. In other words, the neoplastic cells proliferate in their normal habitat, hence the name "*in situ*" (Latin for "in its place"). For example, carcinoma *in situ* of the skin, also called Bowen's disease, is the accumulation of neoplastic epidermal cells within the epidermis only, which has failed to penetrate into the deeper dermis.



For this reason, CIS will usually not form a tumor. Rather, the lesion is flat (in the skin, cervix, etc.) or follows the existing architecture of the organ (in the breast, lung, etc). Some CIS, however, do form tumors, such as in the colon (polyps), in the bladder (pre-invasive papillary cancer), or in the breast (more properly called ductal carcinoma in situ).

Many forms of invasive carcinoma (the most common form of cancer) originate after progression of a CIS lesion. Therefore, CIS is considered a precursor or incipient form of cancer that may, if left untreated long enough, transform into a malignant neoplasm.

When explaining a laboratory report to a patient, most doctors will refer to CIS as "pre-cancer", not cancer. However, because most forms of CIS have a high probability of progression into invasive carcinoma, doctors will usually recommend that the lesion be completely removed. Therefore, CIS is usually treated in much the same way as a malignant tumor.

In the TNM classification, carcinoma *in situ* is reported as T*is*N0M0 (Stage 0).

Dysplasia vs carcinoma *in situ* vs invasive carcinoma

These terms are related since they represent the three steps of the progression toward cancer:

- Dysplasia is the earliest form of pre-cancerous lesion recognizable in a biopsy by a pathologist. Dysplasia can be low grade or high grade (see CIS below). The risk of low-grade dysplasia transforming into cancer is low.
- Carcinoma in situ is synonymous with high-grade dysplasia in most organs. The risk of transforming into cancer is high.
- Invasive carcinoma, commonly called cancer, is the final step in this sequence. It is a disease that, if left untreated, will invade and spread to surrounding tissues and structures of the host (hence its name), and may eventually be lethal.

Examples

- Many bladder cancers are CIS.
- Cervical cancer is often predated by cervical *squamous intraepithelial lesion* (SIL, previously CIN, a form of dysplasia). The term CIS is not used for the cervix. Instead, the term *high grade SIL* (HSIL) is used (essentially a synonym). It is this lesion that is detected with the smear.
- Ductal carcinoma in situ (DCIS) of the breast is a rather frequent disease with a high probability of transforming into true breast cancer if left untreated.
- Bowen's disease is squamous carcinoma *in situ* of the skin.
- Colon polyps often contain areas of CIS that will almost always transform into colon cancer if left untreated.
- High grade prostatic intraepithelial neoplasia is equivalent to CIS of the prostate.
- Bronchioloalveolar carcinoma (BAC) of the lung is the only form of CIS that can kill directly because, in rare cases (the "pneumonic form"), it expands greatly and fills the lungs, preventing breathing and causing other dire effects on the host. Thus, the pneumonic form of BAC is a true malignant entity, but is not "invasive" in the classical sense. For this reason, it is considered a form of CIS by pathologists, but not by oncologists or surgeons and inclusion of this form of cancer among the types of CIS is controversial.

- Lentigo maligna (also known as "Lentiginous melanoma on sun-damaged skin") is a melanoma *in situ* that consists of malignant cells but does not show invasive growth. Lentigo maligna is not the same as lentigo maligna melanoma, and should be discussed separately. It typically progresses very slowly and can remain in a non-invasive form for years. The transition to true melanoma is marked by the appearance of a bumpy surface (itself a marker of vertical growth and invasion), at which point it is called lentigo maligna melanoma. Incidence of evolution to lentigo maligna melanoma is very low, about 2.2% to 5% in elderly patients.

- Barrett's oesophagus, sometimes called Barrett syndrome or columnar epithelium lined lower oesophagus (CELLO), refers to an abnormal change (metaplasia) in the cells of the lower portion of the esophagus, where the normal squamous epithelium lining of the esophagus is replaced by goblet cells (cells usually found lower in the gastrointestinal tract). It is considered to be a premalignant condition because it is associated with an increased risk of esophageal cancer

Treatment

Carcinoma in situ is, by definition, a localized phenomenon, with no potential for metastasis unless it progresses into a "true" cancer. Therefore, its removal eliminates the risk of subsequent progression into a life-threatening condition. Some forms of CIS (e.g. colon polyps and polypoid tumours of the bladder) can be removed using an endoscope, without conventional surgical resection. Dysplasia of the uterine cervix is removed by excision (cutting it out) or by burning with a laser. Bowen's disease of the skin is removed by excision. Other forms require major surgery, the best known being intraductal carcinoma of the breast (also treated with radiotherapy). One of the most dangerous forms of CIS is the "pneumonic form" of bronchioloalveolar carcinoma of the lung, which can require extensive surgical removal of large parts of the lung. When too large, it often cannot be completely removed, with eventual disease progression and death of the patient.

The Blood Safety and Quality Regulations 2005 No. 50

PART 3 ELIGIBILITY CRITERIA FOR DONORS OF WHOLE BLOOD AND BLOOD COMPONENTS

Deferral criteria for donors of whole blood and blood components

2.1. Permanent deferral criteria for donors of allogeneic donations

Cardiovascular disease	Prospective donors with active or past serious cardiovascular disease, except congenital abnormalities with complete cure
.....	.....
Malignant diseases	Except in situ cancer with complete recovery