TRANSPLANTATION OF ORGANS
FROM DECEASED DONORS
WITH CANCER OR A HISTORY OF CANCER

April 2014
Recommendations

1. Organs from deceased donors with some cancers may be safely used for transplantation. On the basis of the current evidence, it is recommended that organs from deceased donors with some current and past cancers may be safely used.

2. Risks of cancer transmission must be balanced against the risks of dying without transplantation. The risk of inadvertent tumour transmission has to be balanced against the risks of non-use of the organs and the risk of a patient dying awaiting a graft or becoming too sick for the procedure to be successful. This decision should be made by the recipient surgeon having considered and discussed the risk/benefit with the patient. The surgeon may seek the advice of colleagues; there should be clear records of such discussions.

3. The risk of donor-transmitted cancer in the UK is currently 0.06%. Transmission of a previously undiagnosed cancer from a donor to a recipient does occur and potential transplant recipients should be advised that current UK data (2001-10) suggest that this risk (i.e. where the presence of the cancer was not known before or at the time of retrieval and implantation) is less than 1 in 2,000 organs transplanted.

4. Past or current donor cancers can be divided into contra-indicated, higher and lower risk. Characteristics of these cancers are summarised in the Tables below.

5. Potential recipients must give informed consent. Surgeons must ensure that the recipient has given informed consent, which should include the understanding that transplanted organs may rarely transmit cancer and that organs from some donors with a history of current or past cancers may be used. Where potential donors have a cancer that is associated with a higher risk of cancer transmission, the surgeon may wish to discuss use of these organs with colleagues and seek specific consent from the intended recipient.

6. Recipient wishes must be respected. If a potential recipient does not wish to receive an organ from a donor with cancer, this should be made clear at listing rather than at the time of offering. The recipient should be allowed to change their mind without detriment to their care.

7. The retrieval team should make every effort to exclude previously recognised cancer or cancer spread during the retrieval process. The retrieval team should, wherever appropriate, undertake a full review of the imaging reports available prior to retrieval (and, if expertise permits, the imaging itself) and, during the retrieval process, should perform a full examination of the abdominal and thoracic cavities.

8. Histological characterisation of all tumours prior to implantation is desirable although it is recognised that in some cases, it may not be feasible to delay implantation until the histology reports are available. It should also be appreciated that histological assessment based on rapidly
fixed specimens is less reliable than assessment after full examination following full fixation and sometimes after additional staining.

9. **NHS Blood and Transplant (NHSBT) should maintain a register of outcomes of transplants from donors with cancer.** The need for clinicians to identify and report when organs from donors with current or past cancers are used and for NHSBT to maintain a registry and report outcomes is self-evident.

10. **The risk of transmission from donors with Central Nervous System (CNS) tumours is 1.5%.** The overall risk of cancer transmission from deceased donors with a CNS tumour is 1.5%. For high-grade tumours (e.g. Glioblastoma) the risk has been estimated to be around 2.2%. The presence of a cerebrospinal fluid shunt will increase the risk of extra-neural metastasis but this is estimated at less than 1%.

11. **The optimal management of patients in whom a high risk donor cancer has been identified after implantation or when there is evidence of cancer transmission is uncertain.** The decision whether to remove the organ, modify immunosuppression and/or offer chemo- or radiotherapy will depend on the type of cancer, the organ transplanted and the interval between transplantation and recognition of the cancer, and should take into account the recipient’s wishes.
Introduction

The number of people who would benefit from a solid organ transplant is increasing, as more people develop end stage kidney, liver, heart, lung, pancreas or bowel failure. Although the UK, as many other countries, has seen an increase in the number of deceased donors, the rate of increase has failed to match the increase in the need for a transplant. Furthermore, the quality of the organs retrieved is falling, as donors become higher risk because of increasing age, increasing obesity and the greater use of organs from donors after circulatory death. The rate of death on, or removal from, the waiting lists (which is up to 20% for heart, lung and liver candidates) underestimates the short fall. Although some immunosuppressive agents have the potential to promote tumour spread, others, such as sirolimus and everolimus, have anti-neoplastic effects and so the choice of immunosuppressive regimen may mitigate the consequences of donor cancer transmission.

Organs donated by deceased donors carry many risks and these include transmission of infection and cancer. Cancers in the recipients may be divided into donor transmitted cancers and donor derived cancers. Donor transmitted cancers are those cancers which are present in the transplanted organ and tissue whereas donor derived cancers are those that are of donor origin but develop in the graft after transplantation. Differentiation between these two cancers may be difficult and is usually dependent on time after transplantation. These should be distinguished from recipient cancers which may be present before or develop after transplantation.

Donor assessment will allow some evaluation of the risks but the limitations of diagnostic imaging, especially in the clinical context of donation, mean that while these risks can be minimised, they cannot be abolished. The donor assessment team has the responsibility of ensuring as full an assessment as possible is made within the constraints around the donation process, and the recipient surgeon has the responsibility of deciding whether to accept the donated organ(s) for that patient. The responsibilities of the surgeon are described in detail elsewhere (1). It is important that the potential recipient is adequately counselled about the risks involved (as well as the benefits) and gives an informed consent.

To provide guidance to surgeons and patients, several organisations have published recommendations, using a variety of databases and different classifications (see Table 1). The Council of Europe Guidelines (2) classify some donors as having an unacceptable risk whereas the UNOS guidelines (3) follow a similar classification as the UK, defining donors with a high or lower risk of tumour transmission. Nalesnik and colleagues (4) suggested six levels of tumour transmission risk from nil to high (>10%). For those donors with high risk, it was recommended that use of organs from such donors should be discouraged except in rare and extreme circumstances, and that informed consent was required.

These recommendations for patients in the UK are based on a review of the UK National Transplant Registry and a review of the literature. However, it
must also be appreciated that these recommendations are made on evidence from those donors with cancer that have donated and therefore there will be inherent biases which may affect the conclusions from the reviews of past activity.

We have classified the risk of cancer transmission into the following categories:

- Absolute contra-indication
- High risk (>10%)
- Intermediate risk (between 2% and 10%)
- Low risk (between 0.1% and 2%)
- Minimal risk (<0.1%).

It must be recognised that these categories are somewhat arbitrary and will need regular review as more evidence becomes available.

**Cancers in potential donors**

Data from the Potential Donor Audit of patients who died between 1 October 2009 and 31 March 2013 (3.5 years) identified that 4,208 out of 27,465 potential DBD (donation after brain death) and DCD (donation after circulatory death) donors were contraindicated because of 'any malignancy within the past 12 months, excluding brain tumour'. To analyse further the type of cancer, a subgroup of 2,886 potential donors who died in the 5 months between 1 April 2013 and 31 August 2013 were examined; there were 452 potential donors who were contraindicated due to cancer. Of these, 338 had cancer with evidence of spread outside the affected organ within the three years preceding death, 107 had active haematological malignancy, 5 had melanoma other than completely excised stage 1 cancer and 2 had chorioncarcinoma. DBD potential donors were those with apnoea, coma from known aetiology, fixed and dilated pupils and being ventilated, while DCD potential donors were those with treatment withdrawn where death was anticipated within four hours. It should be noted that these data do not account for cancers that were not contraindicated.

**Cancers in consented, eligible donors from the Core Donor Data Form**

Between 1 April 2003 and 31 March 2013, there were 506 donors with 'tumour' indicated in their medical history, or for whom cancer was indicated as a cause of death. 358 of these had at least one organ transplanted (a further 17 donated but no organs were utilised). Thus, these donors make a small but significant contribution to the number of organ transplants and outcomes for patients.

**Recipients who developed donor-transmitted cancer**

The UK experience of donor-transmitted cancers (DTC) was published in 2012 (5). A DTC is one that was present in the donor, perhaps unknown, which spreads to the recipient using the transplanted organ as the vector. It may appear first in the donor organ, or remote from it. From 14,986 donors
there were 30,765 transplants between January 1 2001 and December 31 2010. Eighteen recipients developed cancers of donor origin; organs were from 16 donors (0.06%). Of these cancers, 3 were donor-derived cancers (0.01%). A donor-derived cancer is one that develops de novo in the donor organ. 15 were cancers that were donor-transmitted cancers (0.05%). Of these 15 DTCs, 6 were renal cell cancer, 5 lung cancer, 2 lymphoma, 1 neuro-endocrine cancer and 1 colon cancer. These recipients underwent explant/excision (11), chemotherapy (4), and radiotherapy (1). Of 15 recipients, 3 (20%) recipients with DTC died as a direct consequence of cancer. Early diagnosis of DTC (diagnosed within 6 weeks of transplantation) was associated with a better outcome (no DTC-related deaths in 11 cases) compared with late recognition of DTC (DTC-related deaths in 3 of 4 cases). Five-year survival was 83% for kidney recipients with DTC compared with 93% for recipients without DTC (p=0.077). None of the donors from whom cancer was transmitted were known to have cancer at donation. The authors concluded on the basis of these data that the risk of inadvertent transmission of cancer was small and cannot always be avoided.

**Donors with Primary CNS tumours**

Based on a UK review of 448 recipients of organs from 177 donors with primary CNS tumours without any evidence of tumour transmission (6), recommendations for the use of organs from potential donors with CNS tumours were published (7). The data were obtained by reviewing the outcomes of 246 UK recipients of organs from donors with CNS tumours. It was concluded that use of such donors increased survival by an average of 8 years. These have been included in the overall recommendations above.

**Donors with non-CNS tumours**

The risk of cancer transmission from those UK donors with a history of non-CNS tumours was recently analysed. Of 17,639 donors, 202 (1.15%) had a history of cancer including 61 donors with cancers classified by the Council of Europe Guidelines (2) as contraindicated “except for vital urgencies”. No cancer transmission was noted in 133 recipients of organs from these 61 donors. At 10 years from transplantation, the additional survival benefit gained by transplanting organs from donors with unacceptable/high risk cancer was 944 life-years (95%CI 851, 1037) with an average survival of 7.1 years (95%CI 6.4, 7.8) per recipient. Thus it seems reasonable to use organs from selected donors with cancers, and comparable conclusions were reached by others (8).

Based on the UK experience and review of extensive registry data, we classify cancers in potential donors as absolute contraindications, or carrying a high, intermediate, low or minimal risk of transmission (Table 2).

Based on the limited data available, it is not possible to determine whether some donor organs are less likely to be associated with cancer transmission than others.
Although the presence of active haematologic malignancy is an absolute contraindication, low grade malignancies may need further consideration. Included in this group are monoclonal gammopathy of uncertain significance (MGUS), Polycythaemia vera (PV), Essential thrombocythaemia (ET) and monoclonal B cell lymphocytosis (MBCL). Median survival with PV and ET is in the region of 20 years (9), and with MGUS (10) and MBCL (11) is in the region of 13 years. The behaviour of pre-existing MGUS in the recipient does not seem to be affected by transplantation or its associated immunosuppression (12). These cancers which have a long median patient survival may have to be viewed in the context of patients’ need for organs. Discussion with a local expert in haematological malignancy is advised.

Management of the recipient after implantation of an organ from a donor where cancer transmission is possible

Recognition that a donor has a cancer may be made after implantation of an organ. We have identified situations where recognition of such an event has occurred when the donor has a fuller autopsy, when there has been a fuller review of the histology of a suspected lesion, when an organ has been biopsied for other reasons (such as determination of rejection) or when a tumour has developed in one recipient and histological and other information has shown this to be of donor origin.

Recommended actions to be taken when a cancer is identified in the donor after donation or when an instance of donor-transmitted cancer is confirmed or suspected

- The clinicians must immediately inform the national transplant organisation so that clinicians looking after other recipients can be informed and management modified as appropriate.
- All recipients of organs from that donor should normally be informed.
- Under the EU Organ Donation Directive, inadvertent transmission of donor cancer is classed as a Serious Adverse Event or Reaction and should be formally reported to NHSBT.
- There should be a formal review to determine whether the transmission could have been prevented and to ensure any lessons learned are shared.
- We recommend that the national transplant organisation should maintain a registry so that all donors with cancer can be identified; and that the outcomes of transplants from such donors should be published at regular intervals (such as 5 yearly) so guidelines can be refined. Such a registry should also include details of how the recipient was managed and the recipient outcome.

Recipient management

While there are several case reports in the literature, there are few large series on which to base any recommendations about management, and many factors will determine the optimal management for an individual case:

- Type of tumour: the natural history of the cancer (such as whether it is likely to metastasise early) and whether it is responsive to treatment (with chemo- or radio-therapy)
• **Organ transplanted:** for example, a kidney can be removed and the patient supported with dialysis whereas a heart recipient may need to wait for another suitable donor

• **Time after transplant:** anecdotal evidence, where the organ has been removed after only a few hours, suggests that cancer transmission and metastasis can occur within hours of implantation

• **Immunosuppression regimen:** most immunosuppressive agents will enhance the growth of cancers; however, the mTOR inhibitors (sirolimus and everolimus) have anti-neoplastic properties and are effective in the treatment of some cancers (e.g. renal cell carcinoma). It seems sensible to recommend minimising immunosuppression and considering the benefits of switching to an mTOR inhibitor-based regimen. Alternatively in kidney transplantation, cessation of all immunosuppression has been reported to result in the immune-mediated destruction of some tumours.

**Minimisation of the risk of transmission**

While it is accepted that it is inevitable that some cancers will be inadvertently transmitted because of the nature of the donation process, steps to minimise the likelihood should include:

• A full review of all information available at the time of donation (as is current practice)

• A full exploration of the thoracic and abdominal cavities during or at the end of the retrieval process

• Histological examination of unexplained lesions prior to implantation. It must be recognised that it is not always possible to provide a full 24/7 expert histological assessment of material in a timely fashion and that conclusions from rapidly fixed specimens and without the benefit of special stains may, even in expert hands, lead to erroneous conclusions.

**Further recommendations**

• NHSBT should maintain a register of donors with a past or current history of cancer, and all actual and possible cases of donor transmitted cancers, and publish outcomes on a regular basis.

• All health care professionals should be reminded of their obligations to report to NHSBT any case of possible or actual donor transmitted cancer as soon as such a cancer is recognised.
Table 1. Recommendations on the use of organs from donors with CNS tumours

**Absolute contra-indications**
- Primary cerebral lymphoma
- All secondary intracranial tumours.

**Intracranial tumours with an intermediate risk of cancer transmission**
(2.2% with an upper 95% CI of 6.4%) include WHO grade 4 tumours and equivalents:
- Glioblastoma
- Giant cell glioblastoma
- Gliosarcoma
- Pineoblastoma
- Medulloblastoma
- CNS primitive neuroectodermal tumour
- Medulloepithelioma
- Ependymoblastoma
- Atypical teratoid/rhabdoid tumour
- Malignant peripheral nerve sheath tumour
- Germinoma
- Immature teratoma
- Teratoma with malignant transformation
- Yolk sac tumour
- Embryonal carcinoma
- Choriocarcinoma.

**Intracranial tumours with a low risk of transmission** (<2%) include WHO grade 3 and equivalents:
- Anaplastic astrocytoma
- Anaplastic oligodendroglioma
- Anaplastic oligoastrocytoma
- Ependymoma
- Choroid plexus carcinoma
- Anaplastic gangliomyoma
- Pineal parenchymal tumour of intermediate differentiation
- Papillary tumour of the pineal region
- Malignant peripheral sheath tumour
- Anaplastic/malignant meningioma
- Papillary meningioma
- Rhabdoid meningioma
- Haemangiopericytoma.
Table 2. Recommendations on the use of organs from donors with non-CNS cancers

**Absolute contra-indications**
- Active cancer with spread outside the organ
- Active haematological malignancy.

**High risk (>10% risk of transmission)**
- Melanoma: without spread (except as below)
- Breast: cancer other than those identified below
- Colon: cancer other than those identified below
- Kidney: renal cell cancer >7cm or stages 2-6
- Sarcoma: >5 years previously and resected
- Small cell cancer: lung/neuroendocrine
- Lung cancer: stage I to IV.

**Low risk (0.1-2% risk of transmission)**
- Melanoma: superficial spreading type with tumour thickness <1.5mm with curative surgery and cancer free period of >5 years
- Breast: stage 1, hormone receptor negative with curative surgery and cancer-free period of >5 years
- Ovary: curative surgery and cancer-free >10 years
- Colon: adenocarcinoma with curative surgery and cancer-free period of >5 years
- Thyroid: solitary papillary carcinoma 0.5-2.0cm
- Thyroid: minimally invasive follicular carcinoma 1.0-2.0 cm
- Kidney: resected solitary renal cell carcinoma >1.0cm and <2.5 cm and Fuhrman grade 1/2
- Prostate: Gleason >6
- Treated gastrointestinal stromal cancers.

**Minimal Risk (<0.1% risk of transmission)**
- Skin: basal cell carcinoma
- Skin: squamous cell carcinoma with no metastases
- Skin: non-melanoma skin cancer in situ
- Uterine Cervix: in situ cancer
- Thyroid: solitary papillary carcinoma (<0.5cm)
- Thyroid: minimally invasive follicular carcinoma (<1.0cm)
- Bladder: superficial non-invasive papillary carcinoma
- Kidney: Resected solitary renal cell carcinoma <1.0cm and Fuhrman grade 1/2
- Prostate: Gleason <6 or >6 with curative treatment and cancer free >3 years.

**Note.** Only those cancers where evidence is available for analysis have been classified. Cancers not included in this guidance should be considered on a case by case basis following appropriate professional consultation.
References


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