

NHSBT-TES POSITION STATEMENT

The Risk of Transmission of the SARS-CoV-2 Virus via Tissue Allografts

July 2020

Background

Coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, emerged in December 2019 in Wuhan, China. The World Health Organization (WHO) has declared on 11th March 2020 that the outbreak of COVID-19 is a pandemic, based on the high level of global spread and severity. COVID-19 is an acute respiratory disease caused by a single-stranded RNA virus.

SARS-CoV-2 is a respiratory virus, which normally affects the airways. There is limited data available regarding the presence of viable virus in blood, bodily fluids and various tissues and organs. Therefore, evaluation of the risk of transmission of COVID-19 via tissues allografts must consider the potential presence of the virus in specific cells, how such infected cells could be distributed in tissues and organs, and the potential for viraemia resulting from donor blood in vascularised tissues. SARS-CoV-2 invades host cells via interaction of its spike protein with membrane receptor ACE2.

Evidence published during the early stages of the pandemic based on data collected from symptomatic individuals shows that the detection rate for viral nucleic acid in blood ranged from 15% (1) to 1% (2). More recently there is limited published information available on viraemia in the incubation period, during asymptomatic infection, or after the resolution of symptoms. The Wuhan Blood Centre reported (3) on the identification of 2 RNA positive donations from asymptomatic donors, and 2 RNA positive donations from pre-symptomatic donors out of a total of 7,445 tested (0.05%). No data has been published on the follow up of these cases and whether or not they were confirmed true positives

To date only viral nucleic acid, not infectious virus, has been found in blood (virus has not been cultured from blood samples taken from laboratory confirmed infected individuals) and hence the presence of viral RNA does not necessarily equate with infectivity of tissue allograft. There is one report from Korea where transfusion of platelets obtained from an infected individual who had not yet developed signs and symptoms of COVID-19 did not result in disease transmission, even though, the platelet recipient was diagnosed with very severe aplastic anaemia and was taking immunosuppressive drugs (4).

The Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) Standing Advisory Committee on Transfusion/Transplantation Transmissible Infections (SAC-TTI) have updated their position statement for COVID-19 for blood, tissue and cell transfusion and transplantation. This updated version takes into consideration the guidance in European Centre for Disease Control (ECDC) risk assessments (5) and evidence in the scientific data which is accumulating at a rapid pace. (6)

There have been no documented cases of transmission of SARS-CoV-2 or similar viruses, (SARS-CoV and MERS-CoV), through transplantation or transfusion. Therefore, based on currently available knowledge and taking into account the processing applied to the majority of tissues, the risk of

COVID-19 transmission via tissue allografts is theoretical. However, the presence of SARS-CoV-2 RNA in the bloodstream of some infected individuals, and the expression ACE2 receptor in tissues does indicate the need for a risk assessment to provide assurance on control measures.

Tissue Risk Assessments

In performing these tissue risk assessments, there are certain risks and mitigations that are common to all tissues, and some that are specific to individual tissues, based on specific processing protocols. The primary risk that needs to be considered is that tissue will be retrieved from an asymptomatic donor who is infected with COVID-19, that viable virus will be present in donated tissues, and that the virus will survive any processing protocols and be transmitted to the recipients of the donated tissues. Although viral RNA has been detected in organs and tissues from deceased donor tissues who died of confirmed SARS-CoV infection, viable virus was only successfully isolated in culture in lung and intestine samples (7).

This document will first address generic risk mitigations, and then address in detail any additional mitigations afforded to different types of tissue by the processing applied. In the context of this report, the term 'processing' applies to any treatments applied to the tissue during retrieval (procurement), subsequent processing in the tissue bank, and post-process decontamination and storage protocols. Finally, based on the totality of the evidence, a recommendation will be made for each type of tissue as to whether or not it can be considered to have undergone an inactivation procedure with respect to SARS-CoV-2.

Generic Tissue Safety Measures

Donor Selection : Respiratory viruses are not known to be transmitted via tissue allografts, however until the pathogenesis of this new Coronavirus is known, precautionary measures are being applied; any potential tissue donor with confirmed or suspected COVID-19 infection will not be accepted until at least 28 days after the symptoms have resolved. There is also a generic deferral of 14 days from recovery for any donor with systemic acute infection. Similarly, restrictions are applied to potential donors who may have been in contact with a person with confirmed or suspected COVID-19 (8,9) infection, cannot donate for at least 14 days unless they themselves have tested negative.

Donor Testing: There are currently no validated tests available for screening respiratory or blood samples from deceased tissue donors for SARS-CoV-2. In the UK, organ donors are currently tested pre-mortem for SARS-CoV-2 by combined nose/throat swab and endotracheal aspirate and are accepted with a negative nucleic acid testing (NAT) result. Therefore, tissue donors who are also organ donors are tested for SARS-CoV-2 RNA.

Currently, there is no consistency in international practice with respect to screening tissue donors for COVID-19. The ECDC issued updated guidance on the risk of SARS-CoV-2 transmission via substances of human origin on 30th April 2020 (5). They have recommended that

- Living and deceased tissue donors with active, confirmed Covid-19 are not eligible for donation
- Living and deceased donors who have recovered from confirmed Covid-19 may donate tissues at least 14 days after laboratory evidence of viral RNA clearance from the upper respiratory tract, or 28 days after resolution of symptoms.
- Donors who have contact with infected individuals are not eligible for donation until at least 14 days after the last contact if they do not develop symptoms

- For deceased donors, without symptoms or diagnosis of Covid-19, who have lived in or visited areas of sustained community transmission of the virus, tissues should not be collected unless the donors test negative for the presence of SARS-CoV-2 RNA in the upper or lower respiratory tract in specimens collected within 72 hours prior to retrieval, or the tissues collected will be treated with a disinfection, sterilisation or microbial inactivation procedure validated to inactivate enveloped viruses.

In line with these recommendations, tissue specific risk assessments have been performed and the outcomes are summarised in Appendix 1.

Retrieval & Processing: Tissue allografts generally undergo processing, decontamination and preservation protocols to prepare them for short- or long-term storage. Many of these processes have antiviral properties. Depending on the process in question, these can reduce or eliminate the theoretical risk of viral transmission via tissue allograft transplantation. For example, there is evidence that treatment with biocidal agents such as ethanol, povidone iodine and hydrogen peroxide inactivate coronaviruses at the concentrations that are used in routine tissue allograft retrieval and processing protocols. Some tissues are also sterilised with high dose gamma irradiation, which has been shown to inactivate coronaviruses. The efficacy of the methodologies used in retrieval & processing, and their potential impact on viral inactivation or removal thereby on the tissue safety, are summarised in Appendix 1. During retrieval and processing activities, staff observe strict aseptic technique, use personal protective equipment, and work in controlled processing environments to minimise the risk of contamination of the donated tissue from the environment.

Clinical Use: In contrast to solid organ transplants, most tissue allograft recipients do not routinely require immunosuppression, and therefore these grafts are unlikely to pose additional risk to recipients. Clinicians will be aware of other co-morbidities that put their patients at higher risk of severe COVID-19 and are expected to assess any risk accordingly. Hospitals should communicate post-transplant infection in recipients, in accordance to established procedures for reporting post-transplant serious adverse event/reactions.

Current activity: During the initial phase of the Covid-19 outbreak in the UK, planned non-emergency procedures were suspended in NHS hospitals (since late March/early April). This reduced the clinical requirement for tissue allografts, with transplants restricted to urgent procedures such as emergency heart valve and cornea transplant. Since the beginning of June, hospital trusts are initiating a recovery program to re-introduce planned surgical activity. NHSBT-TESS is implementing a complementary recovery plan to support this anticipated increase in activity.

Since March 2020, living donor programs for bone and amniotic membrane have been suspended to ease pressure on NHS hospitals. It is likely that patients undergoing planned procedures will have been screened for SARS-CoV-2 through respiratory swabs and tested negative prior to surgery. There is no additional requirement to screen these donors, they will be advised to report post-donation illness if they develop any symptoms of infection.

Review of Grafts in Stock: SACTTI has identified the 28th February 2020 as the date from when the UK is to be considered a country with sustained community transmission of SARS-CoV-2. On this date, the first case of COVID-19 transmitted in the UK was identified. An individual risk assessment will be required to determine the suitability for clinical use of donations taken place after 28th Feb that are still in quarantine, in line with the risk assessment detailed in Appendix 1.

Summary

I) It is our position that the processing steps applied to corneas, sclera, processed bone, massive allografts, tendons (irradiated & decontaminated), irradiated skin, decellularised dermis, meniscus and osteochondral grafts are sufficient to remove or inactivate enveloped viruses.

II) It is our position that the processing steps applied to heart valve, artery and cryopreserved skin grafts are **not** sufficient to remove or inactivate enveloped viruses.

Review

This document will be reviewed no later than one month from the date of preparation as specified below, or sooner if and when relevant new information regarding SARS-CoV-2 and COVID-19 becomes available.

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Appendix 1: Overall risk score for COVID-19 transmission by different tissues

The table below summarises the risk scores calculated by the detailed risk assessments detailed in Appendix 2, on a scale of 1 to 30. A score of 10 or below indicates that we are satisfied that sufficient processing is applied to the tissue to remove/inactivate any SARS-CoV-2 that may be present. Note that the risk assessment is based on worst case assumptions, specifically that an asymptomatic donor may be viraemic, that the SARS-CoV-2 virus could infect and replicate in different tissues, and that viable virus may be present in donated tissues. There is currently no data confirming productive infection outside the respiratory tract and no data exists on minimum infectious dose through a non-respiratory route.

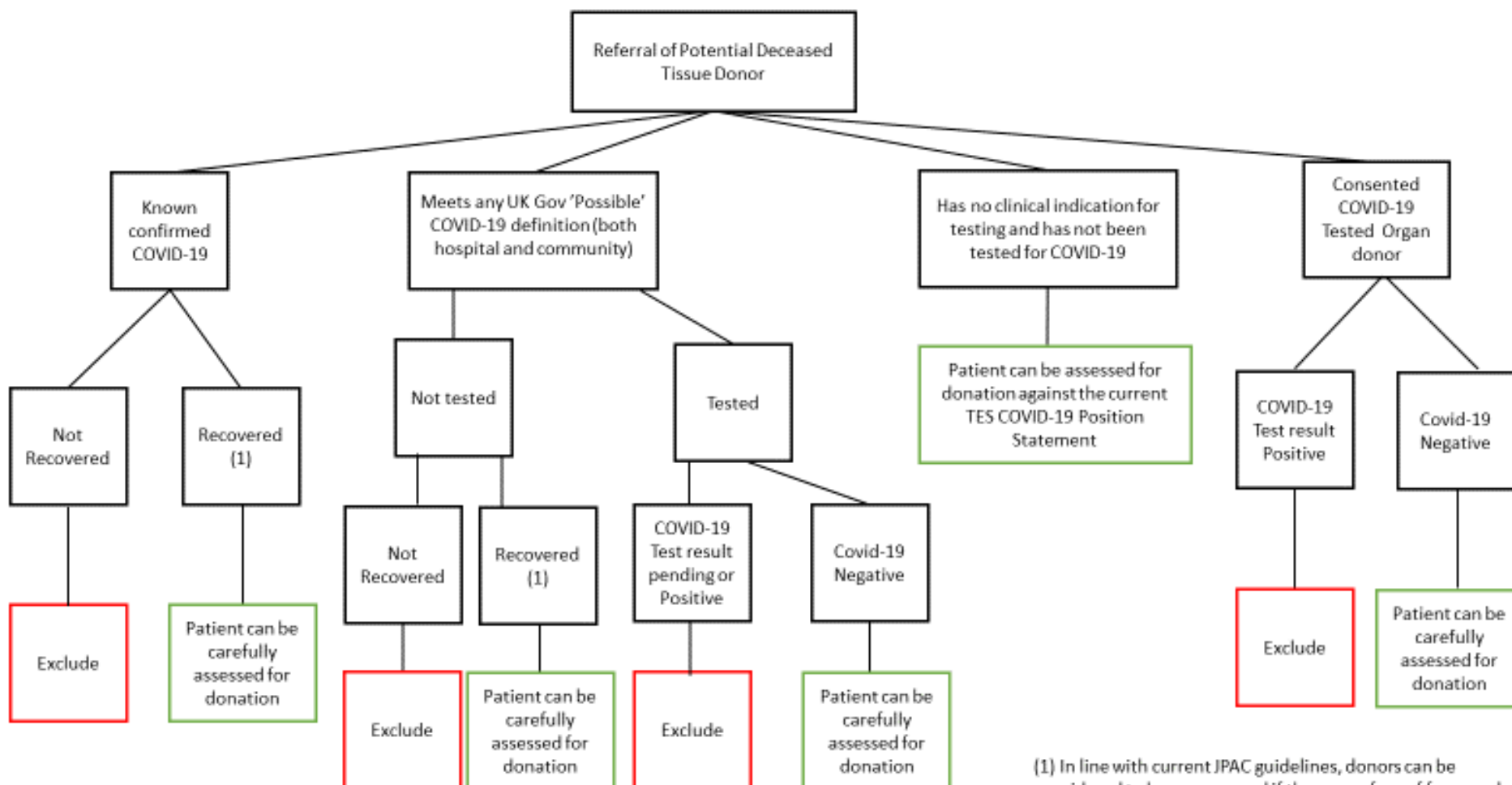
Tissue Type	Risk that SARS-CoV-2 could be present in the tissue at the point of retrieval	Could SARS-CoV-2 proliferate in the tissue (presence of the ACE2 receptor)	Level of viral risk reduction achieved by processing	Overall Risk Score*
Cornea	1	2	1	2
Sclera	2	2	1	4
Skin (cryopreserved)	3	2	3	18
Skin (irradiated)	3	2	1	6
Processed bone	1	2	1	2
Massive allografts	1	2	1	2
Tendon (decontaminated)	1	2	2	4
Tendon (irradiated)	1	2	1	2
Heart valves	2	2	4	16
Arteries	2	2	4	16
dCELL dermis	3	2	1	6
Meniscus	1	2	4	8
Osteochondrals	1	2	4	8

* Calculated by multiplication of individual risk factors

Risk Scoring

Risk that the tissue could be contaminated with SARS-CoV-2	Vascularised tissue – 1, heavily vascularised tissue – 1, exposed to surface contamination – 1. (score is additive; range 0-3, 0 = no risk)				
Risk that SARS-CoV-2 could proliferate in the tissue	No- 1		Yes - 2		
Level of risk reduction achieved by processing	Negligible -5	Low -4	Moderate -3	Significant - 2	High -1
Overall Risk Score	Calculated by multiplying the three scores				

Appendix 2: Testing Flowchart



(1) In line with current JPAC guidelines, donors can be considered to have recovered if they were free of fever and respiratory symptoms for 28 days at the time of death