Clinical Commissioning Policy
Fresh osteochondral allograft for osteochondral lesions of the knee in adults and post-pubescent children [221003P] (2007)

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Commissioning position

Summary

Fresh osteochondral allograft is recommended to be available as a routine commissioning treatment option for osteochondral lesions of the knee within the criteria set out in this document.

The policy is restricted to certain age groups as it is not recommended to be used in those age groups not included in the policy.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Executive summary

This policy proposes that fresh osteochondral allograft (OCA) be made available as a treatment option to adults and post-pubescent children who have osteochondral lesions greater than 2cm^2 in size. The potential exists for significant cost savings given that without treatment, osteochondral lesions will deteriorate over time and progress to osteoarthritis with the potential to result in significant physical and psychological impairment.

The main alternative surgical treatment for osteochondral lesions is autologous chondrocyte implantation (ACI). When ACI is used in osteochondral lesions, bone grafting to replace the missing bone is initially performed upon which the ACI is then placed. The results of ACI combined with bone graft are inferior compared to ACI alone. Unlike ACI alone and OCA, where 15-20 year data exists, there is minimal long-term data to evidence the efficacy of ACI combined with bone graft.

In cases where cartilage repair is no longer feasible, the only remaining treatment option is total joint replacement, a procedure with low satisfaction rates (60-70%) and high revision rates in patients under 50 years.

Plain language summary

About osteochondral lesions

Osteochondral lesions are combined lesions of cartilage and bone, usually within the knee. The main symptoms involve pain, swelling, instability (giving way) and locking (when the knee becomes fixed in one position). As a consequence, patients are unable to stand for long periods, walk significant distances or undertake manual work. Without treatment these lesions progress, become larger and result in osteoarthritis (OA). The condition also impacts negatively on patients' mental health due to their pain and inability to function.

About current treatment

The current treatment for an osteochondral lesion is a 2-stage process:

1. The first stage involves a knee arthroscopy, during which a sample or biopsy of healthy cartilage is taken. The cartilage biopsy is sent to a laboratory where the cartilage cells (chondrocytes) are extracted and grown.
2. After around 6 weeks later a second operation occurs to implant the cells. First, the diseased or absent bone is replaced with bone graft and then the cells are placed on top.

About the new treatment

Fresh OCA is a surgical technique for treating patients who have significant cartilage and bone (osteochondral) lesions in their joints. Usually the knee joint is affected. Healthy bone and cartilage obtained from young, recently deceased donors, is implanted to repair the cartilage and bone damage in a single surgery. The purpose of OCA is to improve pain and function in patients with osteochondral lesions and to delay the need for artificial joint replacement e.g. total knee replacement (TKR).

What we have decided

NHS England has carefully reviewed the evidence to treat osteochondral lesions of the knee in adults and post-pubescent children with fresh OCA. We have concluded that there is enough evidence to make the treatment available at this time.

Committee discussion

Clinical Panel considered the evidence presented supported the policy continuing with a routine commissioning position.

See the committee papers (link) for full details of the evidence.

The condition

There are 3 principal causes of lesions of cartilage and bone within the knee (osteochondral lesions):

1. Osteochondritis dissecans: a condition that usually presents in the teenage years and onwards, where a piece of bone and cartilage becomes detached from the joint surface of the femur (thigh bone). In the majority of cases, the lesions are small but in a small proportion of people the lesions can be very large, involving half the entire joint surface of the knee.
2. Trauma: Fracture of the femoral condyle or tibial plateau (joint surface of shin bone), which can result in significant cartilage and bone loss despite surgical intervention.
3. Avascular necrosis (AVN): This occurs when there is damage to the blood supply of the bone just underneath the joint surface, resulting in bone death and subsequent collapse of the joint surface. AVN can be caused by a number of medical conditions (e.g. sickle cell disease), drugs (e.g. steroids, chemotherapy, alcohol) or metabolic disorders. These lesions

commonly affect young patients, in whom without treatment, secondary osteoarthritis develops.

Cartilage lesions may deteriorate over time, increase in size and progress to OA. With effective early treatment, OA can be potentially prevented. The subgroup of patients with osteochondral lesions are therefore a clinical priority given that deterioration of the osteochondral lesion may reach a point where the cartilage repair of the lesion is no longer feasible and the only other main treatment option is joint replacement.

Patients suffering from osteochondral lesions have been shown to be as disabled as those suffering from severe OA. Consequently, this younger population have significant impairment of activities of daily living. The burden of joint disease not only affects patients physically but also has a detrimental effect on mental health. Psychological distress is more frequently experienced by patients with OA compared to patients with diabetes. Psychological sequelae include distress, devalued self-worth, and loneliness.

Physical and psychological impairment leads to a significant socioeconomic burden secondary to absence from work and disability. OA results in loss of economic production of over £3.2 billion per year and a further £215 million is spent on social services and £43 million on community services. Effective treatment in this patient group can reverse these symptoms and consequently have a substantial positive effect for the individual and for society as a whole.

Current treatment

The current treatment for osteochondral lesions is a bone graft and ACI[1]. When there is significant bone damage, for example after traumatic injury, the bone lesion requires a bone graft to replace the missing bone, before the cartilage layer can be repaired. The results of ACI combined with bone graft, a method known as the 'sandwich technique', are inferior compared to ACI alone. There is little long-term data available on ACI plus bone graft compared to ACI alone and thus the long-term survival is unclear. In certain situations where the bone loss is towards the back of the femoral condyle, unlike OCA, it is technically impossible to undertake a bone graft and ACI.

The non-biological option would be a partial or total joint replacement. The 17th annual report of the UK National Joint Registry shows that in 2019 there were 108,506 knee replacements undertaken, plus 7,008 revision knee procedures. The results of TKR in patients under the age of 50 have a satisfaction rating of 60 to 70% percent, with some patients complaining of persistent pain and functional limitations on a daily basis. In patients under the age of 55, the 10-year revision rates are over 35%. Therefore, in younger patients with osteochondral lesions cartilage repair is preferable in order to delay joint replacement and the need for future revision surgery.

From a clinical perspective, revision knee surgery is a complex procedure associated with high complication rates, extended hospitalization, unsatisfactory functional outcomes, and a relatively shorter survival compared to primary procedures. In particular, revision TKR due to infection costs twice as much as aseptic revision, is associated with poor patient outcomes, and, in some cases, can lead to arthrodesis or amputation.

Proposed treatment

Fresh OCA is a surgical technique to treat patients with significant bone and cartilage damage in joints, most commonly the knee. The technique relies on obtaining healthy tissue from young recently deceased donors and transferring it to the damaged area of the recipient's knee. The donor tissue needs to be implanted within 28 days of donation in order to maintain cartilage cell

[1] Following NICE approval in October of 2017, ACI has become the standard treatment for cartilage lesions in the knee greater than 2cm^2. This 2 stage technique involves an initial arthroscopy where a small cartilage biopsy is taken. The cartilage cells (chondrocytes) are extracted from the tissue and placed into culture. The cells are multiplied many times and then implanted at a second procedure approximately 6 weeks later.

viability in excess of 70%, thus providing better long-term outcomes. The donor bone and cartilage can be transferred in one of 2 ways. For well-defined areas of cartilage damage in easily accessible areas,1 or 2 cylinders of bone and cartilage (up to a maximum diameter of 30mm) can be transferred using specialist instrumentation. For more extensive areas of damage, larger segments can be cut and shaped freehand. Using cadaveric tissue eliminates the donor site morbidity associated with osteochondral autografting (using bone and cartilage tissue from within the patient's own knee) and allows for the treatment of larger and more aggressive lesions. The technique also allows for the ability to implant fully formed articular cartilage in a single-stage procedure. Osteochondral allografting to the knee has been reported in the literature for more than two decades with graft survivorship in the femoral condyles estimated to be 95% at 5 years and 85% at 10 years. The aim of the procedure is to improve pain and function in adults and post-pubescent children and to delay the need for TKR. In the USA, 3000 allografts are implanted each year with good effect. The use of OCA in England would enable severe lesions to be treated, thereby reducing the incidence of early onset OA and the need for early TKR. This policy proposes that OCA should be accessible to patients via specialist tertiary centres as there is significant unmet patient need.

New devices to support OCA are not commissioned by NHS England. The companies who supply the allografts are located in the USA and have distribution agents in the UK with whom NHS providers have a service level agreement. Laboratory testing takes place on the allograft donors in the USA. The distribution agents have Human Tissue Authority (HTA) licences and, in accordance with HTA guidelines, ensure that a coroner's report is formalised for each allograft before its release to the NHS provider organisations. In the event that the graft does not arrive at the NHS hospital by the scheduled time, the UK distributor refunds the NHS provider with the allograft cost.

Due to the limited availability of OCA there can be a significant delay whilst an appropriately sized graft is identified. Consequently, ACI should be the primary treatment for chondral lesions greater than $2cm^2$. OCA should be reserved for osteochondral lesions greater than $2cm^2$, which may take the form of a cartilage lesion in association with bone loss or bone disease (for example, bone death due to avascular necrosis). Osteochondral lesions vary in severity and clinical judgement determines when the bone disease requires replacement.

Epidemiology and needs assessment

NICE TA477 estimated that around 500 patients per year would require treatment for cartilage lesions greater than $2cm^2$ in the knee. A proportion of these large lesions would also have significant associated bone abnormalities and would therefore be better suited to treatment with OCA. Whilst the true figure is unknown, an estimate in the region of 50 patients per year in England out of the 500 would benefit from this intervention.

Evidence summary

An independent evidence review was conducted for fresh osteochondral allograft. NHS England has concluded that there is sufficient evidence to support a policy for the routine commissioning of fresh osteochondral allograft for osteochondral lesions of the knee in adults and post-pubescent children. The evidence review which informs this commissioning position can be accessed here.

Implementation Criteria

Inclusion criteria

To be eligible for treatment, patients should be post-pubescent and have all of the following:

- An osteochondral lesion greater than $2cm^2$.
- A well aligned, stable knee
- A functioning meniscus

- No significant OA[2]
- Kellgren Lawrence scale grade score less than 3 (minimal osteoarthritic damage).

The criteria that should be used to determine whether ACI or OCA is the most appropriate surgery are presented in Table 1 below.

ACI	**OCA**
Lesions 2cm^2 or greater	Lesions 2cm^2 or greater
Chondral lesion – no significant bone abnormality	Osteochondral lesion – significant diseased bone or bone loss
Osteochondral lesion - when a delay waiting for OCA might result in patient deterioration	Failed prior microfracture or osteochondral repair

Table 1: Criteria used to determine whether ACI or OCA is the most appropriate surgical intervention

Exclusion criteria

Patients who meet the following criteria are not eligible for treatment with fresh OCA:

- Patient is suitable for ACI
- Pregnant women
- Adolescents whose growth plates have not yet fused
- Patients currently requiring oral steroids
- Ongoing metabolic bone disease

Starting criteria

The patient has been discussed in an MDT meeting[3] with a minimum of 3 orthopaedic surgeons present and a consensus has been reached that the patient is not suitable for ACI. The MDT decision will be recorded and is auditable.

Stopping criteria

The OCA procedure will not take place if any of the following apply:

- The graft size does not match the recipient
- The allograft does not meet the quality required by the Human Tissue Authority (HTA) guidelines[4]
- The allograft is not received on time to allow donor tissue to be implanted within 28 days of donation
- The allograft has not been appropriately stored.[5]

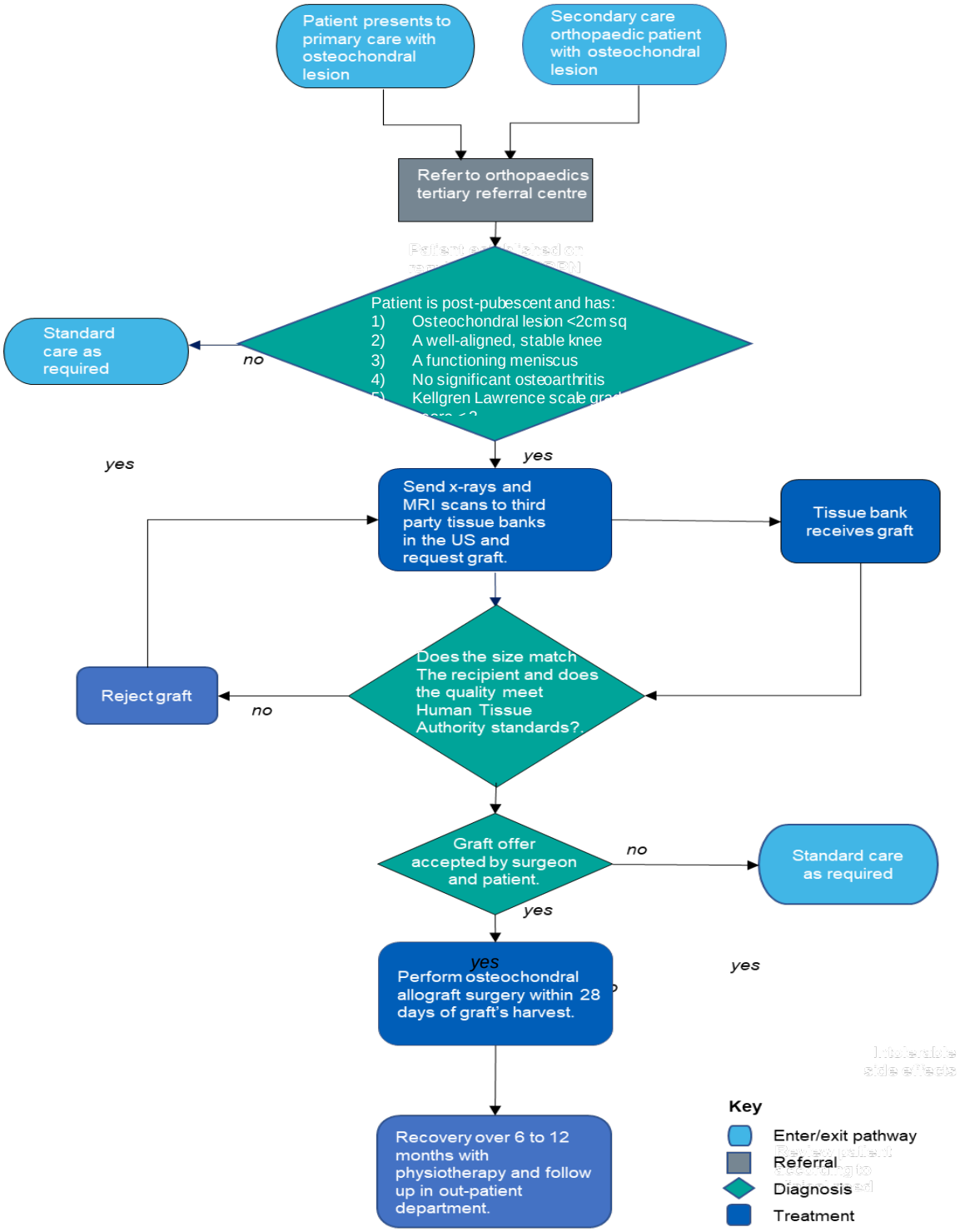
[2] In patients with significant osteoarthritis, the results of cartilage repair are generally considered to be inferior compared to the results in patients who do not have significant osteoarthritis. The reason is that the chemical environment within the knee of a person with significant osteoarthritis is not conducive to repair. However, there are some exceptional cases where the results would not be inferior, for example, post traumatic lesions in young person.

[3] OCA will only be undertaken in hospitals where ACI is also performed. Currently there are 5 centres in the UK where OCA surgery could potentially take place:

[4] The HTA standards Annex A, section 1. describe the criteria for exclusion of a donor; Annex B, paragraph 1. describes the laboratory tests required for donors and Annex B, paragraph 2 describes the general requirements for determining biological markers.

[5] For international shipments of allografts FedEx or DHL will be the courier. The recommended storage temperature for fresh allografts is 1˚ to 10˚C. The allografts should not be exposed to freezing temperatures or heat. Storage/transport boxes have a 150-hour time period. It is advised that the allograft is left within the box until surgery, if within expiry date of box. This avoids any storage issues or graft mishandling. Fresh allografts are stored in a nutrient medium. Following removal of the packaging, the allografts are flushed to remove storage media, blood and marrow elements using high-pressure lavage with an isotonic solution. The allograft should be kept moist with a cold or room temperature sterile isotonic solution until time of transplant.

Patient pathway



Governance arrangements

Tertiary centres must abide by the HTA 2004 regulations. The tertiary centres should hold their own HTA licence or have a service level agreement with a HTA approved supplier of human allograft.

Provider organisations must register all patients using prior approval software and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined. The OCA will be done at a specialised orthopaedic tertiary referral centre which has

been identified by the regional teams and is recognised by NHS England and NHS Improvement as a specialist cartilage treatment centre.

Mechanism for funding

Fresh OCA for osteochondral lesions of the knee in adults and post-pubescent children will be commissioned and funded by NHS England under existing arrangements.

Audit requirements

There are a number of Patient Reported Outcome Measures (PROMS) which are used to assess functional outcomes of cartilage repair. The main PROM recommended by the International Cartilage and joint Restoration Society (ICRS) is the Knee Injury and Osteoarthritis Outcome Score (KOOS). Failure of a cartilage procedure is usually defined as return of PROM score to within 10% of the pre-operative value or the need for revision surgery (further cartilage repair or TKR). The outcomes of cartilage repair, similarly to joint replacement, are commonly judged over a 10-year period.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

Allograft	An **allograft** is transplant of an organ or tissue from one individual to another of the same species with a different genotype. For example, a transplant from one person to another, but not an identical twin, is an **allograft**.
Arthrodesis	**Arthrodesis,** also referred to as a joint fusion, is the uniting of two bones at a joint using surgery.
Arthroplasty	**Arthroplasty** is a term used to describe a surgical procedure to repair or replace a damaged or diseased joint.
Arthroscopy	**Arthroscopy** (also called **arthroscopic** or keyhole surgery) is a minimally invasive surgical procedure on a joint in which an examination and sometimes treatment of damage is performed using an **arthroscope**, an endoscope that is inserted into the joint through a small incision.
Bone graft	**Bone grafting** is a surgical procedure that uses transplanted **bone** to repair and rebuild diseased or damaged **bones**.
Cartilage	**Cartilage** is a resilient and smooth elastic tissue, rubber-like padding that covers and protects the ends of long bones at the joints.
Chondral	A **chondral** lesion refers to a focal area of damage to the articular cartilage (the cartilage that lines the end of the bones).
Dowel	A bone **dowel** is a circular **bone** graft harvested with special instruments used in orthopaedic surgery.
Femoral condyles	The **femoral condyles** are the two rounded prominences at the end of the femur or thigh bone.

Metabolic disorders	A **metabolic disorder** is **a disorder that** negatively alters the body's processing and distribution of macronutrients such as proteins, fats, and carbohydrates.
Osteoarthritis	**Osteoarthritis** (OA) is a degenerative joint disease that causes joints to become painful and stiff.
Osteonecrosis	**Osteonecrosis** can be caused by disease or by severe **trauma**, such as a fracture or dislocation, that affects the blood supply to the bone, causing it to die.
Revision surgery	In **revision surgery**, the surgeon removes some or all of the parts of the original knee replacement prosthesis and replaces them with new ones.
Sickle cell disease	**Sickle cell disease** (**SCD**) is a group of inherited blood disorders. The most common type is known as sickle cell anaemia (SCA) which results in an abnormality in the oxygen-carrying protein haemoglobin found in red blood cells.

Reference

1) NICE. Autologous chondrocyte implantation for treating symptomatic articular cartilage lesions of the knee. Technology appraisal guidance [TA477]. 2017. Available from: https://www.nice.org.uk/guidance/ta477

2) HTA Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. 2021 Available from: https://www.hta.gov.uk/