National Institute for Health and Clinical Excellence

EOS ultra low dose 2D/3D x-ray imaging system for postural assessment (EOS low dose)

Diagnostics Assessment Report (DAR) – Stakeholder comments

Responder reference no.	Comment no.	Page no.	Section no.	Comment	Response from Centre for Reviews and Dissemination (CRD), University of York - External Assessment Group
1	1	26	3.2	Limitation to weight bearing comparators is not appropriate since several studies demonstrate that 3D information can be necessary. Such information is unavailable with CR/DR but available with CT (and EOS). Therefore, CT should be introduced as a comparator. See for instance: in the spine: Hong et al, Spine 2011 Feb 15 (epub ahead of print) In the lower limb: Jaarsma et al Arch. Orthop. Trauma Surg (2004) oct; 124(8):552-4; Moussa et al Clin. Othop. Relat. Res. 1994 (304):176-83 ; Jakob et al, JBJS 1980;62:238-42	The final scope by NICE for the diagnostic assessment of EOS 2D/3D X-ray imaging system is limited to comparators where an upright weight-bearing position can be achieved. CT requires the patient to be recumbent which can result in changes in spinal positioning. The NICE scope explicitly states, "The use of CT scans and conventional MRI were excluded from the evaluation based on comments at the scoping workshop about the ineffectiveness of non-weight bearing on the utility of the imaging." The scope is defined by NICE and not by the EAG. Our understanding is that CT is not routinely used for the monitoring of scoliosis or the other orthopaedic indications
1	2	26	3.3, first paragraph	We suggest that radiation exposure concern should not be a necessary condition. We suggest to consider imaging that benefits from weight bearing , full body, simultaneous PA and LAT and/or 3D and/or where radiation exposure is a concern	The sentence has now been appropriately edited. Radiation exposure was not considered as a necessary condition. All available evidence on the clinical effectiveness of EOS was considered. The inclusion of evidence was not restricted on the basis of whether radiation exposure was a concern or not.
1	3	27	Table 3.1	We suggest to add M16 coxarthrosis, M17 gonarthrosis, M21.7, M21.8, M21.9 acquired deformities of limbs. O32 maternal care for	It is impossible to define every possible indication where EOS could be used. The indications defined in the NICE scope were discussed in detail with clinical experts and a list of indications was developed. Table 3.1 summarises the indications into broad categories by

				none or mal presentation of fetus. O34 maternal care of none or suspected abnormality of pelvic organs. On M16-21 see Follinais et al, SOFCOT 2010 on EOS in lower limb applications On O32-34, see Delin et al, communication JFR2010 and IRSN on EOS for pelvimetry	ICD-10 codes, where EOS is most likely to be used. Given the impossible task of capturing every possible indication where EOS could be employed, threshold analysis was used to capture any additional throughput from indications where EOS is used at the margin.
1	4	27		We do not understand why lower limb applications in the adult have been excluded. See for instance EOS applications in the lower limb: Guenoun et al, EFORT: this communication has been excluded on the basis of not conventional Xray control: however, it compares EOS 3D info versus what is commonly measured in 2D, here with EOS 2D being taken as a conventional DR benchmark Follinais et al, SOFCOT 2010	Lower limb applications in adults have not been explicitly modelled. As noted above, it is an impossible task to define every possible indication where EOS could be used. The threshold analysis based on level of throughput gives an insight into the magnitude of utilization and benefit needed from 'other' indications for EOS to be considered cost-effective.
1	5	30	3.3.5	In this paragraph, we recommend that arthritis and pelvimetry are taken into account.	See comments above about marginal uses of EOS.
1	6	30	3.4	As mentioned in comment #1 CT can be necessary to obtain 3D information, see Hong et al, Spine 2011 Care pathways on the low limb should be added.	See response to comment #1 regarding the exclusion of CT. See response to comment #4 regarding lower limb applications.
1	7	33	3.5.4	As stated above, 3D information is required in some cases and can be obtained with CT or chosen not to be not available due to CT irradiating costs. We therefore suggest to include the following: - Irradiation benefit from not performing a CT exam (see Delin et al above; see	See response to comment #1 regarding the exclusion of CT. Our understanding, on the basis of discussions with the clinical advisors and SCMs, that 3D imaging is not routinely requested for the indications of interest. There is no evidence to suggest that information obtained from 3D images leads directly to improvements in health benefits. Threshold analyses were used to assess the necessary size of the effects, over and above those from reduced radiation, for the technology to be

				Follinais et al above; see Hong above) - Obtention of 3D information that would be unavailable. 3D clinical value is recognized by the Scoliosis Research Society which has appointed a 3D subcommittee. Also see also 3D data prognosis value (Parent et al, submitted to Eurospine Journal) - Higher precision of measurements when performed in 3D: for instance, *measurement of the Cobb angle has limitations in that it is performed by using a two-dimensional radiographic image of a 3D deformity and does not take vertebral rotation into account*. Kim et al, "Scoliosis imaging: what radiologists should know." Radiographics 30 (2010): 1823--1842.	considered cost-effective. The reference to Kim et al has been misquoted. See page 4 of Kim et al (2010): "Measurement of the Cobb angle has limitations in that it is performed by using a two-dimensional radiographic image of a 3D deformity and does not take vertebral rotation into account. In addition, Cobb angle measurement may be inherently difficult (11). **However, it is still the main standard for diagnosis, monitoring, therapeutic planning, and epidemiologic analysis of scoliosis.**"
1	8		3 .6	We suggest to introduce benefits associated with 3D, see above	See response to comment #7 above.
1	9	37	4.1.2.2	The criterion of controlled studies has led to the exclusion of several medical demonstrations. This criterion is appropriate for well established technologies but appears to be very restrictive for innovative technologies. Founding the analysis on only 3 publications out of the 120 studies identified, many of them peer reviewed, reduces dramatically the scope and benefit analysis.	We identified 110 papers/documents that appeared to relate to EOS. Upon inspection of the full publications, 27 were found to be unrelated to EOS, only 22 were excluded because they were not a controlled study. In the vast majority of cases, these publications were editorials and overviews of EOS, rather than uncontrolled studies. Further details of reasons for exclusion are presented in 'Table of excluded studies with rationale' (see end of this document). This additional detail allows the reader to see that none of the excluded studies would have added relevant data to the systematic review.
1	10	37	4.1.2.2	EOS should be accepted as a DR when EOS 3D data is compared with EOS 2D data (example: Humbert 2009) As stated before, CT should be considered a comparator for EOS	This comment is unclear. It is not the objective of this assessment to compare EOS 2D to EOS 3D imaging. See response to comment #1 regarding the exclusion of CT.

1	11	37	partici pants	Criteria relative to participants are very restrictive. In particular, it is appropriate to consider phantom studies for dose measurements which are performed on phantoms in order to minimize patient risk during such studies. Besides, CT dose being measured at the organ cannot be measured on patients	Of the 110 papers/documents that appeared to relate to EOS, 27 were excluded because they did not include orthopaedic patients. The majority of studies were of bones from cadavers. Given that we identified and included 3 controlled studies of EOS in live orthopaedic patients, the inclusion of poorer quality study designs would not have added any relevant good quality data to the systematic review. Further details of reasons for exclusion are presented in 'Table of excluded studies with rationale' (see end of this document).. See response to comment #1 regarding the exclusion of CT.
1	12		4.1.3.2	Again, very restrictive criteria reduce the argument to dose considerations	See response to comment #2 above. The inclusion of evidence was not restricted on the basis of whether radiation exposure was a concern or not.
1	13	68	4.3	There is no reference in this chapter to "willingness to pay" studies, which bring another frame to the economics of radioprotection. See for instance AIEA website	Economic evaluations of EOS against any comparators were considered. No 'willingness to pay' studies were identified. The EAG followed the guide to the methods of technology appraisal by NICE.
1	14	72	4.4.1	Again, comparing to CT would bring a significant change in the outcomes of this argument, both in cost and dose considerations	See response to comment #1 regarding the exclusion of CT.
1	15	75	4.5	Again, the model inputs should include CT as well as lower limb indications	See response to comment #1 regarding the exclusion of CT and response to comment #4 regarding lower limb applications.
1	16	87	Table 4.10	Indicated costs of cancer are based on unpublished data based on personal communications with experts. These data show significant discrepancies with NCI published data on cost of cancer.	The costs of cancer came from comprehensive cancer models, estimated from the point of cancer diagnosis to death. Personal communication was made with the experts that developed these models so that the models could be run appropriately to provide the estimates required. The reference list has now been updated to include publications relating to these models. Campbell HE, Epstein D, Bloomfield D, Griffin S, Manca A, Yarnold J, Bliss J, Johnson L, Earl H, Poole C, Hiller L, Dunn J, Hopwood P, Barrett-Lee P, Ellis P, Cameron D, Harris AL, Gray AM, and Sculpher M. The cost-effectiveness of adjuvant chemotherapy for early breast cancer: a comparison of no chemotherapy and first, second, and third generation regimens for patients with differing prognoses. Submitted to European Journal of Cancer, 2011. Fenwick E, Kulin NA, Marshall D, Hall Long K. A probabilistic decision model to guide optimal health policy decisions for lung cancer screening [presentation HSR-51]. Med Decis

					Making 2011; 31(1):E89. NCI data refer to the US and not to the UK setting.
1	17	89	4.5.6	Assumption was that of identical staff requirements for CR and EOS. Alison et al, ESPR 2009, shows a 4min total exam time for EOS when CR exam times are assumed at 16 min (Table 17 footnote, also uncontrolled). This study has at least the same value as the presented CR data.	Three alternative assumptions regarding patient throughput were considered in the analysis. Throughput assumption 2 was based on a capacity of 30 patients per working day, corresponding to approximately 16 minute appointment slots for both EOS and CR. Throughput assumption 3 was based on a capacity of 48 patients per working day for EOS compared to only 30 patients per working day for CR. It is important to note that there is a difference between the time it takes to capture the image and the number of feasible appointments/utilisation of an EOS machine in a working day. The ability to have 4 minute appointment slots per working day (as opposed to 4 mins to take the image) is highly implausible (particularly with children and less mobile patients). The 16 minutes for CR refers to total appointment time and not to the 'seconds' that it takes to capture the image.
1	18	94	Patient Throughput	Estimates from Table 4.14. relate to episodes of stay and not to radiological procedures. As mentioned in the report, this table severely underestimates the volume of radiographs. French data from CNAM show an annual volume of full spine Xray in the range of 300,000. Furthermore, since EOS as a DR can perform many types of exams that have not been listed, the costs per exam should not be based only on the limited scope of indications but on global volumes.	Table 4.14 provides an approximation of patient throughput based on available data in the UK for the indications of interest. Data on radiological procedures encompass all possible procedures, for example, taking an X-ray image of the hand, foot etc. There were no data on radiological procedures by type of indication in the UK. Therefore, inpatient and outpatient data for the indications of interest were examined to provide an estimate of the number of X-ray examinations per year in the indications. Since this data could underestimate X-ray utilisation in the UK, alternative throughput estimates (as discussed in response to comment #17 above) were considered. Threshold analysis was also presented to show the level of throughput required from the 'other' indications to achieve a cost-effectiveness ratio of £20,000 and £30,000 per QALY. French data are likely to have limited relevance to the UK setting.
1	19	95		The annual cost of ownership calculation is not explicit and we do not understand the results.	It is common practice to annuitize the capital cost of equipment so that the cost is expressed on an annual basis. See page 75 of Drummond et al (2005). Methods for the Economic

					Evaluation of Health Care Programmes. Oxford University Press. The annual sum, *R,* for a capital investment, *P* , over a period of *n* years (the lifetime of the technology), at an interest rate *i* is given by: A reference to Drummond et al (2005) is added to this section of the report.
1	19	95		The cost calculation per exam is not explicit, in particular regarding staff costs. The results do not reflect the usual fixed costs model outcome.	The assumptions employed to model costs were explicitly stated in Table 4.15, page 93. Staffing costs were assumed equivalent between EOS and standard X-ray. Only differences in the capital cost of the equipment, annual maintenance costs, equipment replacement costs and patient throughput were considered. For example, on page 95, the cost of CR was calculated as follows: (1) Capital cost = £95,000, equivalent to an annual cost of £11,423 (see response to comment #19 above) excluding VAT. Annual capital cost = £13,708 including VAT @ 20%. (2) Annual maintenance costs (£10,000) and equipment replacement (£175/4=£44) = £10,044 (see Table 4.13, page 90) excluding VAT or £12,053 including VAT @ 20%. (3) Patient throughput of 30 patients per working day and assuming 251 working days per year gives an annual throughput of 30*251=7,530 patients per year. (4) Therefore the cost per exam = (£13,708 +£12,053)/7,530 = £3.42.
1	20	95	Table 4.17	As stated before, EOS time of exam is 4 min (Alison et al 2009 and associated comments on the relevance of these data)	See response to comment #17 above.
1	21	97	3)	Same as above in scenario 3	See response to comment #17 above.
1	22	101		We do not understand why achieving the estimated ICERs would require other indications to have the same dose reduction benefits.	If the EOS machine is working at full capacity (throughput is fixed), then to keep the same ICER the benefits from the 'other' indications would need to be the same, or otherwise the ICER would increase.

Table of excluded studies with rationale - Systematic review of the clinical effectiveness of EOS

Study details	Reason for exclusion	Further detail
[70]	Not controlled study	Ongoing study – currently recruiting participants
[71]	Not conventional X-ray control	Ongoing study – currently recruiting participants
[72]	Not controlled study	Powerpoint slides on number of EOS examinations undertaken
[73]	Not controlled study	FDA Marketing Authorisation - not a study
[74]	Not controlled study	Overview of EOS – not a study
Alison (2009)[75]	Not controlled study	Presentation on examination time for EOS
Assi (2007)[76]	Not conventional X-ray control	Feasibility study for 3D X-ray reconstruction in cerebral palsy patients
Aubin (1997)[77]	Not EOS	Not EOS
Azmy (2010)[78]	Not orthopaedic patients	Cadaver specimens. Assessing 3D reconstruction
Barthe (2004)[79]	Not orthopaedic patients	Rats
Baru (1998)[80]	Not EOS	Not EOS
Benameur (2005)[81]	Not EOS	Not EOS
Benameur (2005)[82]	Not conventional X-ray control	Assessment of 3D modelling, rather than EOS
Benameur (2001)[83]	Not conventional X-ray control	Assessment of 3D modelling, rather than EOS
Benameur (2003)[84]	Not conventional X-ray control	Assessment of 3D modelling, rather than EOS
Bertrand (2005)[85]	Not orthopaedic patients	Asymptomatic volunteers. Assessing intra- and inter- observer agreement for 3D reconstruction of rib cage
Bertrand (2008)[86]	Not orthopaedic patients	Duplicate report of the above study
Billuart (2008)[87]	Not orthopaedic patients	Cadaveric specimens. Not a controlled study
Breton (2010)[88]	Not orthopaedic patients	Dry femurs. EOS versus CT and DR. Assessing accuracy of femur length measurement, interobserver agreement and radiation dose
Chaibi (2010)[89]	Not conventional X-ray control	Healthy volunteers and cadavers. Comparing 3D EOS models with CT
Chaibi (2010)[90]	Not conventional X-ray control	French PhD thesis – above study is part of this
Charpak (2005)[91]	Not controlled study	Discussion – not a study
Chateil (2005)[92]	Not controlled study	Discussion – not a study
Cheriet (2007)[93]	Not EOS	Not EOS
Comite d'Evaluation et de Diffusion des Innovations Technologiques (1996)[94]	Not controlled study	CEDIT recommendations – not a study
Comite d'Evaluation et de Diffusion des Innovations Technologiques (2007)[48]	Not controlled study	CEDIT recommendations – not a study
Cresson (2010)[95]	Not orthopaedic patients	Assessment of 3D reconstruction (EOS versus CT). Dry bones – 6 femurs
Cresson (2009)[96]	Not conventional X-ray control	Assessment of 3D reconstruction using CT as control
de la Simone (2010)[97]	Not controlled study	Overview of EOS – not a study
Deschênes[98]	Not controlled study	Powerpoint slides discussing studies we had already identified
Deschênes (2009)[99]	Duplicate publication (abstract for included study)	Duplicate publication
Deschênes (2003)[100]	Not conventional X-ray control	Assessment of 3D reconstruction. Not a controlled study
Depres (2005)[101]	Not conventional X-ray control	Not a controlled study

Douglas (2008)[102]	Not EOS	Not EOS
Douglas (2004)[103]	Not EOS	Not EOS
Dubousset[104]	Not conventional X-ray control	Case study
Dubousset (2005)[105]	Not controlled study	Overview discussing patients from studies we had already identified
Dubousset (2005)[106]	Not controlled study	Duplicate report of above study
Dubousset (2008)[107]	Not controlled study	Description of the technology – not a study
Dubousset (2010)[108]	Not controlled study	Overview – discusses patients from studies we had already identified
Dubousset (2007)[109]	Not controlled study	Description of the technology
Dumas (2008)[110]	Not EOS	Not EOS
Dumas (2004)[111]	Not orthopaedic patients	Dried vertebrae.
Dumas (2003)[112]	Not EOS	Not EOS
Dumas (2002)[113]	Not conventional X-ray control	Assessing 3D reconstruction – not clear if EOS
Dumas (2003)[114]	Not conventional X-ray control	Assessing 3D reconstruction – not clear if EOS
Dumas (2005)[115]	Not orthopaedic patients	Healthy volunteers. Assessment of 3D reconstruction using EOS, rather than assessment of EOS
Gangnet (2006)[116]	Not orthopaedic patients	?Not EOS. Assessing 3D reconstruction using healthy volunteers
Gangnet (2003)[117]	Not EOS	Not EOS
Gille (2007)[118]	Not EOS	Not EOS
Glard (2008)[119]	Not EOS	Not EOS
Glard (2009)[120]	Not EOS	Not EOS
Guenoun (2010)[121]	Not conventional X-ray control	Powerpoint slides. Describes study of EOS versus pangonogram in pre-operative assessment of total hip arthroplasty
Hascall (2002)[122]	Not EOS	Not EOS
Humbert (2008)[123]	Not orthopaedic patients	EOS versus CT in 3 sets of bones from cadavers
Humbert (2009)[124]	Not conventional X-ray control	Controlled part of the study used CT scan
Humbert (2008)[125]	Not conventional X-ray control	Controlled part of the study used CT scan
Illes[126]	Not controlled study	Case study
Illes[127]	Not conventional X-ray control	Before and after X-rays, no control
Illes (2010)[128]	Not conventional X-ray control	Before and after X-rays, no control. Case study
Janssen (2009)[129]	Not orthopaedic patients	Healthy volunteers. No control
Jolivet (2010)[130]	Not conventional X-ray control	CT control. Healthy volunteers
Journe (2010)[131]	Not orthopaedic patients	Dry bones. CT control
Kadoury (2008)[132]	Not EOS	Not EOS
Kadoury (2009)[133]	Not EOS	Not EOS
Kalifa (1996)[134]	Not controlled study	Editorial – not a study
Lafage (2002)[135]	Not EOS	Not EOS
Laporte (2004)[136]	Not EOS	Not EOS
Laporte (2002)[137]	Not EOS	Not EOS
Laville (2009)[138]	Not orthopaedic patients	Cadavers. No control
Lazennec[139]	Not conventional X-ray control	CT control. Case study
Le Bras (2003)[140]	Not orthopaedic patients	EOS versus CT in dry bones
Le Bras (2004)[141]	Not orthopaedic patients	EOS versus CT in dry bones. Includes most of same patients as above
Le Bras (2002)[142]	Not orthopaedic patients	EOS versus CT in dry bones
Le Bras (2003)[143]	Not orthopaedic patients	EOS versus CT in dry bones
Mitton (2007)[1]	Not orthopaedic patients	EOS versus CT in dry bones
Mitton (2006)[144]	Not orthopaedic patients	EOS versus CT in dry bones
Mitton (2000)[145]	Not EOS	Not EOS
Mitulescu (2002)[146]	Not EOS	Not EOS
National Institute for Health	Not controlled study	Information from manufacturer – not

and Clinical Excellence[2]		a study
Ngoc Hoan (1979)[147]	Not EOS	Not EOS
Node-Langlois (2003)[148]	Not EOS	Not EOS
Novosad (2002)[149]	Not EOS	Not EOS
Obeid[150]	Not conventional X-ray control	Case study
Ohl (2010)[151]	Not orthopaedic patients	Healthy volunteers. No control
Pomero (2003)[152]	Not conventional X-ray control	?Not EOS. Dry bones. No control
Pomero (2004)[153]	Not conventional X-ray control	?Not sure if EOS. CT control
Rillardon (2005)[154]	Not conventional X-ray control	EOS versus MRI on discs (not live patients)
Rousseau (2007)[155]	Not orthopaedic patients	Healthy volunteers. No control
Sabourin (2010)[156]	Not conventional X-ray control	EOS versus CT
Sandoz (2008)[157]	Not orthopaedic patients	Healthy volunteers. No control
Sapin de Brosses (2010)[158]	Not orthopaedic patients	Dry bones. Not a controlled study. Assessing bone mineral density
Sapin (2008)[159]	Not conventional X-ray control	European spine phantom. Assessing bone mineral density
Sapin (2007)[160]	Not orthopaedic patients	European spine phantom. Assessing bone mineral density
Sato (2004)[161]	Not EOS	Not EOS
Sauli (1995)[162]	Not controlled study	Overview – not a study
Schlatterer (2009)[163]	Not conventional X-ray control	Healthy volunteers + 2 knee surgery patients. Not a controlled study
Sebag[164]	Not controlled study	Powerpoint slides on examination time
Situ (2009)[165]	Not EOS	Not EOS
Steffen (2008)[166]	Not conventional X-ray control	Case study. CT control
Steffen (2010)[167]	Not conventional X-ray control	Control was asymptomatic patients
Sudhoff (2007)[168]	Not conventional X-ray control	Assessment of knee attachment systems. No control
Sushkov (2008)[169]	Not EOS	Not EOS
Vital (2008)[170]	Not controlled study	Overview – not a study
Wahrburg (2000)[171]	Not EOS	Not EOS
Zheng (2006)[172]	Not orthopaedic patients	Dry bones. Not clear if EOS
Zheng (2008)[173]	Not orthopaedic patients	Dry bones. Assessment of 3D reconstruction technique, not clear if EOS. Not standard X-ray control

Ends.