Appendix One – Stakeholder/CRG Feedback

Organisation Responding	Feedback Received	PWG response	Resulting Action
Patient	*Recommendation for 6 week public consultation.*		
British Nuclear Medicine Society	Though not a comment, we need to look how this service can be provided across England without a post code lottery of access. The BNMS are willing to help in this process if this is required *Recommendation for a length of public consultation not answered.*	NHS England is the single national commissioner of SIRT and therefore any clinical commissioning policy (for either routine or non-routine commissioning) applies equitably to all patients in England. The selection of commissioned providers takes into account the need to maximise geographical access, alongside other clinical selection criteria.	No action required

Non Profit Professional	*Recommendation for 6 week public consultation.*	Noted	No action required
Oncology Department, University Hospitals, Leicester	*Recommendation for 6 week public consultation.*	Noted	No action required
Individual patient response (Part of the Patient Cabinet at Bury CCG)	Having read the evidence and proposals, I agree that a very important omission is the effect on the patient's quality of life during any extra time they may have gained through this treatment. Most cancer sufferers would want the end of life to be as good as it possibly can be. Providing people are fully informed of potential side effects as well as benefits, it seems that this is a scientific breakthrough that could go further. It is important to be prepared to stop this new treatment if the risks and side effects outweigh the benefits as far as the patient is concerned. Also, there must be a constant review of such treatment with patients as well as clinicians to ensure this is the right course of action. Further, it is essential to look at the very broad spectrum of other cancer research that may provide far improved interventions. *Recommendation for a length of public consultation not answered.*	Noted Data should be captured through the registry database	 Included in the audit requirements
Individual clinician response (Clinician at Oxford	The limit of 5 hepatic lesions is at variance with the majority of the published evidence. It appears based on the CtE figures and whilst the median OS for <5 lesions was longer there is overlap of the confidence limits between the <5 and 5-10 groups. As such the best outcomes in the group with up to 10 lesions is superior to the worst of the patents in the <5 group. It seems unreasonable to deny	The access criteria and treatment protocol within the Commissioning through Evaluation scheme were	Comments noted but no change made to the policy proposition.

University Hospitals NHS Foundation Trust)	those potential good responders treatment on the basis of a single post hoc analysis *Recommendation for a length of public consultation not answered.*	determined jointly with the advice of NICE and lead clinicians, and aimed to capture new evidence to help support future policy determination. A policy proposal does not have to reflect the parameters of a previous CtE scheme but must reflect the available published evidence	
Sirtex Medical United Kingdom Ltd.	**Section 1** With reference to the criteria set out in Section 8, we recommend the final paragraph reads "and have concluded that there is sufficient evidence to make SIRT using resin yttrium-90 microspheres available for adults where the metastatic disease is limited to the liver only." **Section 7 – Conclusions** The CtE registry did not include a comparator group and therefore we recommend the penultimate paragraph reads "Outcomes data (…) in the CtE scheme are in the lower range of published evidence.", removing other statements in this sentence. **Section 8** We believe that the number of liver tumours is not a relevant	Comments noted; no change required. No change	No action required.

	eligibility criterion for patients receiving SIRT, contrary to the absence of extrahepatic disease (EHD) or a tumour to liver volume ratio ≤25% (tumour burden ≤25%). While univariate Cox proportional hazards model of overall survival (OS) based on the SIRT CtE registry have identified statistically significant associations between these characteristics and median OS, no clinically-relevant relationship has been established between treatment with SIRT and the number of liver tumours. Conversely, EHD and tumour burden are clinically relevant because SIRT is a liver-targeted therapy: while limited EHD may not be of prognostic relevance in this setting, extrahepatic lesions cannot be treated with SIRT; furthermore, the administration of SIRT requires a preserved liver function, which may be compromised in patients presenting with a high tumour burden. The absence of EHD and a tumour burden ≤25% have previously been identified as independent predictors of survival outcomes following SIRT with Y-90 resin microspheres in the target indication, e.g. in a systematic review (Saxena 2014, doi:10.1007/s00432-013-1564-4) and two additional cohort studies (Kennedy 2015, doi: 10.3978/j.issn.2078-6891.2014.109; Saxena 2015, doi:10.1245/s10434-014-4164-x). The number of tumours has not been reported as a prognostic factor following SIRT in any study known to Sirtex in this indication. Design flaws of the CtE registry, especially regarding the measurement of OS, prevent interpretation of the outcomes of this study alone, without consideration of published evidence on SIRT with Y-90 resin microspheres. The number of liver tumours may not be considered as an independent prognostic factor as it is strongly correlated with the measure of tumour burden: among patients without EHD and with 1-5 liver tumours in the CtE registry, only 17% also presented with	Noted see above	

	a tumour burden >25%. Furthermore, 95% confidence intervals for median OS estimates between the selected subgroups are largely overlapping, suggesting the absence of difference in survival outcomes between these subgroups. Given the uncertainty surrounding OS estimates in the CtE registry and the strong dependence between covariates for tumour burden and the number of liver tumours, the latter criterion should be discarded in favour of tumour burden, which is both a clinically relevant and documented criterion. Alternatively, patients in the target indication could be considered eligible for SIRT with Y-90 resin microspheres when satisfying one OR the other of these criteria. **Section 11** Please clarify the proposed funding mechanism for resin Y-90 microspheres. Current Tariffs do not cover the costs of this product and require updating, aligned with NHS England routine commissioning. *Recommendation for 12 week public consultation.*	Comments noted. Issue will be considered as part of the impact assessment stage.	
Terumo Europe	"We are concerned about the proposed commissioning criteria listed in Chapter 8 page 23 – and in particular that the treatment with SIRT will be limited to resin yttrium-90 microspheres 1) This would limit clinical and patient choice, UK market competitiveness, as well as access to innovative technologies 1.1 Clinical choice and UK market competitiveness The choice of product to be used depends on clinical preferences, as well as procurement decisions in the different NHS hospitals. If	NHS England is responsible for the commissioning (funding) of SIRT and in determining clinical commissioning policy, follows a formal development and testing methodology which is published on NHS	Comments noted but no changes made to the policy proposition, beyond the description of the material of Quiremspheres.

	commissioning is limited to resin yttrium microspheres (SIR-Spheres®), it would limit the choice available to clinicians and would limit the options available to procurement departments, thereby creating a quasi-monopoly for SIR-Spheres, which would be detrimental to the NHS. 1.2 Access to innovation in the NHS QuiremSpheres® have the same mode of action as existing Yttrium-90 based SIRT products (SIR-Spheres® and Therasphere): the microspheres emit their beta radiation which destroy tumour cells. In addition to emitting the therapeutic beta radiation, holmium-166 emits primary gamma photons and is paramagnetic. The low energy gamma radiation passes through and out of the body and can be directly imaged by gamma-cameras (such as SPECT). This unique property makes it possible to visualise QuiremSpheres® and determine the intrahepatic distribution with high resolution and accuracy, even at low concentrations. In addition, the metal holmium can be visualised with MR imaging. Imaging of the microspheres is of great value for the optimal application of SIRT since it will enable better post-treatment dose verification." "2) The evidence questions in the commissioning policy do not correspond to the SIRT evaluation framework 2.1 The objective of Commissioning through evaluation was to evaluate the SIRT procedure. In the 2013 interim commissioning statement, SIRT is described as a “form of radiotherapy that has been developed for the treatment of unresectable primary and secondary liver cancer”; “a medical device”, “a technique”, “a procedure”. In the report published by CEDAR in July 2017, the central question was summarised by the PICO framework for the SIRT procedure. Never has it been the intent to evaluate the three	England’s website. This includes a requirement to base commissioned treatment options and access criteria on the available published evidence. Commissioned providers are required to work within published policies to ensure equity of access to clinically and cost effective treatments. The PWG agrees that the CtE scheme did not include holmium-166 based treatments and that the CtE results are therefore not generalizable to other forms of SIRT. When CtE was set up Holmium was not available commercially in UK. No centre in UK has	

	different medical devices separately. 2.2 We are disappointed that the SIRT registry, which was the cornerstone of CtE, has been totally ignored to draw the conclusions of this policy proposal." "3) It goes against the recent CtE decision on LAAO from NHS England and NICE statements 3.1 The recent decision by NHS England (9 July) to commission Left Atrial Appendage Occlusion highlights that there are several devices available (Watchman, ACP, and Amulet) but recommends the procedure and not one device over the other (see here) 3.2 NICE already made a statement about Holmium-SIRT as part of their Interventional Procedure process. We received this communication from NICE: • The Interventional Procedure Committee at NICE recently considered if QuiremSpheres should be evaluated separately from previous IP guidance on SIRT [due to the different isotope] and found that “After careful consideration we do not believe that this procedure falls within our remit. This is because this procedure is considered to be a minor modification (variation) of existing procedures, IPG460, IPG401, IPG459, which have already been considered by the Interventional Procedures Advisory Committee”. This gives an indication that any assessment should not consider different technologies separately but as a joint appraisal. [Note: IPG 460, 401, 459 are guidance on safety and efficacy of SIRT for HCC, mCRC and ICC]" 4) All 3 products available (SIR-Spheres, Therasphere and QuiremSpheres) have the same IFU and the same mode of action	experience of using it NHS England criteria may vary from NHS E criteria. Based on the finding of the evidence review there is insufficient evidence available to consider the use of SIRT with Holmium. The original IG410 was specific to Yttrium 90 Include in Stakeholder feedback paper	

	4.1 IFU **3. INDICATIONS FOR USE** QuiremSpheres® is indicated for the treatment of advanced unresectable liver tumors. **3. INDICATIONS FOR USE** SIR-Spheres microspheres are indicated for the treatment of patients with advanced non-operable liver cancer. **INDICATION** TheraSphere™ is used in the treatment of hepatic neoplasia. 4.2 Mode of action All microspheres available have the same mode of action: they emit beta radiation that kills tumour cells from close range. 5) The equivalence of holmium-166 SIRT was concluded by the Dutch Healthcare Institute in the Netherlands (the Dutch Healthcare Institute "Zorg Instituut" is the Health Technology Assessment agency making recommendations about reimbursement in the Netherlands) • In their review of Holmium SIRT published on 9 April 2018, they recommended reimbursement in mCRC (see here) and concluded that "holmium-166 microspheres can be considered as a technical variant of yttrium-90 microspheres" • The evidence review from NHS England released with this policy proposal also describes holmium-166 microspheres as a "a		

	different variation" (Page 4) "Secondly, we are concerned that the population is too restrictive: on page 13, the policy states that "it is estimated that approximately 50 cases would be eligible for treatment with SIRT, in accordance with the clinical criteria set out within Section 8." 1) In the introduction it is mentioned that chemotherapy is the most common treatment in palliative stage liver dominant metastases of CRC but is not ideal because of the severe side effects, and that a new treatment option is needed with better toxicity profile. It is surprising that in such a palliative population with a marginal increase in survival, a well-researched treatment option with a good toxicity profile such as SIRT is so narrowly – almost reluctantly - recommended. 2) The recommendation is for liver-limited only disease. Although the CEDAR report reported that subgroups with liver-limited disease performed better (which is to be expected because of a less advanced disease), it does not mean that for patients with liver-dominant disease SIRT cannot be a valuable treatment option" Lastly we would like to make specific comments about holmium-166 microspheres 1) QuiremSpheres are made of poly-l-lactic acid, not resin (page 9) 2) The policy proposal states on page 18 that No cost-effectiveness evidence was identified in relation to SIRT with holmium-166. However, considering the equivalence of the procedure costs, it can be assumed that the same ICER would apply to holmium-166 microspheres. *Recommendation for 12 week public consultation.*	Differential OS rates and extra hepatic disease is a significant prognostic factor Noted Noted	

Patient	*Recommendation for 12 week public consultation.*	Noted	
BTG plc	1. CtE principles disregarded & questions validity of CtE/use of NHS resources to fund CtE • In this consultation NHSE have totally ignored using NHS funded CtE data – this decision is NOT transparent i. CtE principles were to provide valuable new data beyond that available from clinical trials – so why exclude it now? ii. This sets a future precedence for using CtE data in future NHS decisions iii. By ignoring CtE, glass beads are excluded, & patient selection criteria narrowed – why? iv. Why favour ONE product– If the CtE data is included, with 86% resin and 14% glass and no difference in outcome between products in the analysis, the policy should incorporate all the findings 2. Agree with y90 SIRT only, but disagree with resin y90 only • Resin-only is inconsistent with the 2013 Interim Commissioning Policy & disregards CtE data • CEDAR does not report different outcomes between glass and resin and states that outcomes were consistent with the clinical data in the RCTs included in the review • In clinical practice, glass and resin y90 may be used differently in mCRC patients, depending on the treatment objective e.g. radiation lobectomy versus whole liver treatment • No clinical data available for Holmium nor is it used in the NHS/UK hence not part of CtE. Holmium not the same isotope. Dose efficacy in UK unproven and concern re short half-life and time taken to transport from manufacturing in	The draft policy proposition shared with stakeholders for comment takes into account the available evidence from both the linked CtE and a systematic review of the published literature. Glass and resin were included within the CtE however the evidence review considered both glass and resin microspheres separately. The evidence review found support for the use of resin microspheres but not glass hence exclusion from the initial policy proposition. All other comments noted.	Comments noted but no action taken.

	Netherland 3. Inconsistent application of inclusion criteria for data • If CtE data was included as part of the evaluation, Kennedy & Hickey data should be included (same criteria) • CEDAR report cites CtE data as being consistent with Kennedy. 4. Criteria expansion • Expand to ≤25% burden AND/OR ≤5 tumour - other patients otherwise included in the CtE would be forced into private practice • Include liver dominant - not liver only - disease 5. Disagree with BSC as only comparator • This policy positions SIRT in 3rd line, with BSC as the comparator. This is misaligned with NICE guidance (source: NICE pathways) and current European treatment guidelines (source: ESMO). By definition, only including RCTs vs BSC would exclude the CtE data itself. • The CEDAR report does not mention BSC in the inclusion criteria for its own literature review in the report therefore this policy is inconsistent with the CEDAR review. 6. The exclusion of glass additionally discounts the CtE data, sets precedents for future NICE guidance, commissioning policies and the CtE • Impact on all NICE programmes evaluating medical devices: all IPAC guidance included glass and resin y90 and has assumed that	No standard 3rd line treatment Outside the scope of this policy	

	glass and resin are equivalent based on similar outcomes with clinical data. • This would impact a pending decision by NICE (and the DoH) on conducting either a STA for TheraSphere or an MTA for SIRT, in HCC. • CtE future is questionable – clearly the data from them is not considered when making commissioning decisions. This fundamentally goes against the NHS constitution, Principle 5. 7. CtE data collection • The registry used to collect the data was funded by SIRTEX (resin manufacturers) with data entry biased towards SIR-Spheres e.g. dosimetry was based on body surface area, which is not the same for TheraSphere dose calculation. This took almost 12 months to resolve. • Note: this NHS registry remains on the BSIR website as a proprietary SIRTEX registry which permits the addition of other proprietary products. The promotion of one product over another, unintentional or otherwise, is not appropriate. 8. Policy goes against the NHS Constitution Principle 2: Access to NHS services is based on clinical need, not an individual's ability to pay • Following CtE, many NHS patients are paying to be treated abroad with SIRT, including privately in non-European/Swiss countries and within private UK practice - via doctors involved in CtE. This restricts commissioning criteria beyond the CtE criteria (by eliminating glass and restricting the patient selection criteria) those eligible will have to pay for treatment previously funded by the NHS.	Independent group BSIR ran the registry although funded by SIRTEX Noted Noted see above	

	Principle 5: The NHS works across organisational boundaries See comments under section 5. Principle 7: The NHS is accountable to the public, communities and patients that it serves: "The system of responsibility and accountability for taking decisions in the NHS should be transparent and clear to the public, patients and staff." No explanation or transparency why data for glass y90 is excluded from the commissioning policy despite it having been funded and used in the CtE. The policy breaches patient's right to access health care as defined in the constitution. *Recommendation for 6 week public consultation.*	Noted	
Kings College Hospital NHSFT	"We welcome the proposal and the intention to embed the pathway in the HPB MDT and to limit the procedure to centres appropriately staffed and certificated undertaking sufficient numbers (10-20 cases pa). We are pleased that liver only disease is to be included and would like to see PETCT as the NICE recommendation for assessment. We support the role of the SIRT nurse in the holistic patient care, particularly co-ordination within networked pathways. We are unclear how the proposal for 30 patients pa was developed and how centres will develop. The group is concerned that the recommendations go outside the data collected for the CTE and that some of the recommendations do not appear to be evidence based and need further discussion:	Not included in CtE this change would require PPP submission Based on the ER and CtE numbers	Comments noted but no changes made to the policy proposition.

	We would like to understand why Best supportive care was used as the comparator when the trials have randomised to chemotherapy alternatives and would not be an option if oxaliplatin-based and irinotecan-based chemotherapy failed; particularly as you have chosen 5 liver metastases. We are unclear where this number has been evidenced. We would like to understand why resin yttrium-90 microspheres is intended as the only product when there was no separation in CTE. We recognise the lack of evidence and experience with Holmium. We are not aware of the evidence that radio-embolization should be performed in an interventional radiology suite that is equipped with cone-beam CT. is there an intention to support the implementation of these? We are concerned that, due to the timing of this initial sense check of the proposition that a fuller review period should be considered." *Recommendation for 12 week public consultation.*	CEDAR did refer to BSC See above	
Nottingham University Hospitals NHS Trust	"Page 23 – Would benefit from revision of the spelling / grammatical mistake 'Five of less tumors'. We assume this is "five or fewer tumours". In that instance, is it five or fewer AND ≤ 25%? Or is it five or fewer tumours OR ≤ 25%? Whilst we acknowledge the association between number of hepatic metastases and survival in the analysis of the CtE data, this is a univariate analysis and is likely confounded by tumour burden. The two variables which are supported by published data are presence or absence of extrahepatic disease and intrahepatic tumour burden, number of metastases is not. Whilst presence / absence extrahepatic disease is a binary state and in the gaze of an experienced cross-sectional radiologist,	See above Where a routine commissioning position is recommended the additional investment required will be subject to the twice a	Comments noted but no changes made to the policy proposition

	percentage tumour burden is relatively objective, we are concerned that the number of hepatic metastases is open to interpretation. E.g. one might foresee a situation where 6 metastases comprise 15% of liver volume and on progression, some of these coalesce, creating 3 metastases comprising 25% of liver volume, and therefore less likely to benefit. Indeed it might drive counterintuitive clinical decisions. Those with a miliary distribution of disease, whilst being at higher risk of RILD, seem to respond significantly better than patients with few, but large metastases, as one would expect, given the vascular nature of the therapy. The interpretation of the number of metastases due to complex morphology within patients in the CtE dataset may also undermine the validity of that analysis." "Page 24 – Clarity or further explanation as to funding considerations would be beneficial and useful for service provision considerations. Will there be a nationally agreed tariff? Will providers be given notice of the detail of this ahead of service structuring? Will it be bundled? Who will be the service providers? Any centre proposing to meet those requirements within the described pathway, or those centres recognised within the CtE scheme, or indeed further centralised? *Recommendation for 6 week public consultation.*	year funding prioritisation process for specialised services; the decision making process for this is available on the NHS England website. If the routine commissioning policy is agreed and approved, an implementation plan will be developed. .	
Royal College of Radiologists	"1. Page 23 – Typo - “five of less” should be “five or less” 2. Page 23 – clarification of inclusion criteria - 25% tumour to liver volume or less AND 5 or fewer liver tumours or 25% tumour to liver volume or less OR 5 or fewer liver tumours – the CtE data would support both groups being included equally. 3. The draft commissioning proposition supports only use of resin microspheres. The CtE data was predominantly related to resin	Noted Noted see above	Typing errors amended.

	microspheres (84% versus 16%) but the products were treated the same. No subgroup analysis was planned or carried out looking at the differences between the products and there is no evidence supporting a differential response between these products so this should be at the discretion of the treating clinician. 4. The overall reimbursement for the procedure causes concern. During the CtE programme Trusts were reimbursed £21,550 per course of SIRT. Pennington et al (2017) estimated that each course of SIRT cost approx. £14,248 to deliver. The current tariff reimbursement is unclear as an unbundled brachytherapy tariff is not available and the cost of the microspheres themselves has not been addressed. We are unsure how any Trust will be able to support delivery of SIRT, thus limiting access to this technology unless a national pricing framework for the microspheres is agreed." *Recommendation for 6 week public consultation.*	Noted Noted Noted	
Imperial College Healthcare NHS Trust	"We largely support the clinical commissioning policy on SIRT in the treatment of metastatic colorectal cancer. Our expertise is based on Training/ Mentoring most UK centres in SIRT and as the largest treatment centre in the FOXFIRE study. The proposed pathway criteria are similar to what we use here, but we would also suggest adding one criterion that a minimum of 5 patients/year should be treated with a commissioned centre to keep safety and expertise standards high." "In Section 8 1. The number of liver tumours is not known as a relevant eligibility criterion for patients receiving SIRT and has not been shown to be deleterious in the largest studies. The number of tumours has not been reported as a prognostic factor following SIRT in any study	Noted. Criteria developed as part of the service specification for CtE Noted see above.	No action required.

	known to y90 SIR, in this indication. 2. Limited EHD has not been shown to be of prognostic relevance in this setting, Preserved liver function & PS appear to be the most important factors, which may or may not be compromised in patients presenting with a high tumour burden. 3. The design of capturing efficacy end-points, especially OS in the CtE registry make this difficult to interpret in isolation- other published evidence on SIRT with Y-90 resin microspheres needs to be considered in combination, especially as in the UK we have no access to 5 licenced drugs in CRC, and the SIRT-data in third line and above, appear superior to the alternatives for PFS & TTP, especially in RAS-mutant tumours." "Additionally- over the last 10 years, higher volume centres such as ours are much more selective in offering SIRT to CRC patients and turn down almost 75% of our referrals, and as a result the PFS/TTP and OS data have improved over time. - Although rare (1 in 35-40 in our experience) SIRT can convert some refractory patients to potentially curative surgery - We have no CRC data, or seen sufficient published efficacy or safety data on glass or holmium microspheres to support their use - Right sided colon cancers have an unmet need as they are more chemotherapy-resistant" *Recommendation for 6 week public consultation.*	Extrahepatic disease is a prognostic factor Development of the policy proposition has been based on an evidence review and the findings of the CtE. All studies that met the PICO criteria were considered as part of the evidence review. NHSE can only consider published, peer-reviewed studies. . Noted view regarding the lack of evidence for glass or holmium microspheres	
Nottingham University Hospitals	"The comments below relate to our experiences at Nottingham using each of the products over the last 2-3 years, and specifically focus on the radiation safety of staff ; not any clinical differences.	See above	No action required.

	It appears from the documentation that only the Y-90 labelled resin beads have been approved for funded treatment; It is not clear why the glass version has not been approved. There are several advantages of the glass bead product compared to the resin bead product in terms of safety and ease of use." "• Manufacturers of the glass beads send the patient prescribed activity to the department in a vial so there is no need to dispense a patient specific activity from a stock vial. This has a significant benefit in lowering the radiation dose to staff. We have made measurements of finger dose when dispensing the resin bead product and found that staff can receive as much dose from drawing up one therapy dose as they receive from all their other routine nuclear medicine work in a month. It is part of IRR2017 regulations that doses to staff should be as low as reasonably practicable. • Dispensing the activity also creates a possibility of radioactive contamination; which we have experienced several times. There have been reports from other centres that this activity can become airborne and therefore could present an inhalation hazard to staff. Therefore, consideration needs to be given to operator protection i.e. drawing up in an appropriate safety cabinet. • More radioactive waste is produced from the resin bead product; the activity not used in the stock vial must be stored for several months until it can be disposed of. • The administration of the glass product is 5-10 minutes compared to 15- 30 mins for a resin bead product; this minimises dose to staff in the intervention room. It might be worth considering the number of centres approved to	See above	

	provide this therapy since it is important to maintain competence of staff." *Recommendation for a length of public consultation not answered.*		
Royal College of Physicians (RCP)	The RCP is grateful for the opportunity to respond to the above consultation. We have liaised with the Joint Collegiate Council for Oncology and would like to make the following comments. • On page 5 chemotherapy options should include FOLFIRI +/- Cetuximab first-line • On page 19 median liver specific progression-free survival (PFS) is only 3.7 months. Our experts note that this is of little benefit. • On page 22 PFS and survival do not show a benefit over palliative care. Our experts question whether this is correct and if so, why we would recommend this treatment. • Our experts suggest that percentage of tumour volume would be a better guide than number of lesions on page 23. Small liver lesions are more amenable to treatment. *Recommendation for a length of public consultation not answered.*	The list of regimens is on page 8 Noted This is a direct lift from the report. Para 4.2 p17 of CtE NICE project report. See above	Comments noted but no change required.
Chair of Radiation Oncology (Works at University College London	Typos/clarifications: 1. Page 23- five liver tumours or less (typo on document). 2. Tumour volume of 25 % or less. PROPOSED CHANGE: Based on the NHSE Commisioning through Evaluation data, and to ensure the treatment is offered to	Repeat of RCR submission	No action required.

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<td>Hospitals NHS Foundation Trust)</td>
<td>the appropriate patient group, I would encourage inclusion of patients with ≤25% tumour volume OR ≤5 tumours
(not ≤25% tumour volume AND ≤5 tumours).

Section 11 of the policy proposition is stating that “SIRT, as a form of brachytherapy, is reimbursed though local currencies and pricing arrangements, in accordance with the National Tariff Payment System.”

MAJOR ISSUE: Current tariffs, as defined in the National Tariff Payment System, are not sufficient to cover SIRT costs for NHS Trusts. These tariffs are listed in the table below:

<table>
<tr><th>Phase</th><th>OPCS Procedure codes[1]</th><th>HRG4+</th><th>Elective spell tariff 2018-19</th></tr>
<tr><td>Work-up</td><td>J101 - Percutaneous transluminal embolisation of hepatic artery</td><td>YR54 - Percutaneous Transluminal Embolisation of Peripheral Blood Vessel</td><td>£2,821</td></tr>
<tr><td>Treatment</td><td>J123 - Selective internal radiotherapy with microspheres to lesion of liver</td><td>YR57Z - Percutaneous, Chemoembolisation or Radioembolisation, of Lesion of Liver</td><td>£3,360</td></tr>
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[1] NICE Medtech Innovation Briefing 63 on SIRT with resin microspheres https://www.nice.org.uk/advice/mib63

	Microspheres	SC28Z (unbundled HRG) - Deliver a Fraction of Interstitial Radiotherapy	Not rebundled and no tariffs published
Total funding			**£6,181**

Total funding for both phases of a single SIRT treatment is £6,181, in a base case scenario (elective spell tariff, CC score 0-2).

In comparison, the actual cost of SIRT using Y-90 resin microspheres has been estimated by Pennington et al. (J Med Econ 2015)[2] at £14,248 in total. The total tariff used to reimburse NHS Trusts during the SIRT CtE programme was £21,550.

The current tariffs will therefore not allow NHS Trusts to cover the total cost of SIRT, including the cost of SIR-Spheres Y-90 resin microspheres, with a unit price of £8,000 according to the NICE Medtech Innovation Briefing on this technology.[3]

As a result of this financial consideration, patients eligible for the treatment according to the criteria proposed will not get access to this highly specialised treatment unless the tariffs can be revised.

PROPOSED CHANGE: National Tariffs should be updated for SIRT when it is routinely commissioned and a national currency/price should be defined to cover the unit cost of the product and the technical procedures.

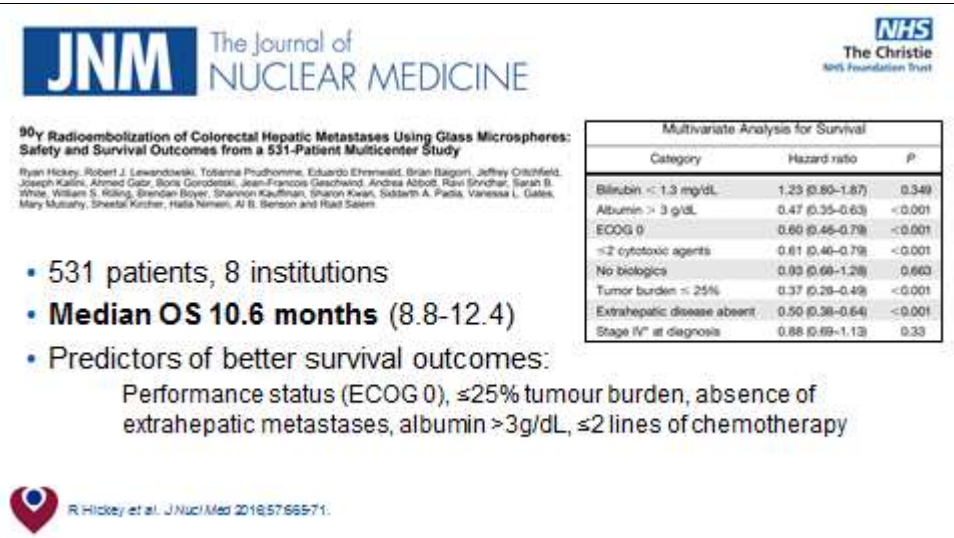
This is being explored as part of the impact assessment

Noted.

[2] Pennington B, Akehurst R, Wasan H, Sangro B, Kennedy AS, Sennfält K, et al. Cost-effectiveness of selective internal radiation therapy using yttrium-90 resin microspheres in treating patients with inoperable colorectal liver metastases in the UK. J Med Econ. 2015 Oct;18(10):797‑804.

[3] NICE Medtech Innovation Briefing 63 on SIRT with resin microspheres https://www.nice.org.uk/advice/mib63

	Recommendation for 6 week public consultation.	Noted	
Consultant Radiologist (Works at The Christie NHS Foundation Trust)	The inclusion of ≤5 tumours in the eligibility criteria is too restrictive. This will prevent access for several patients with ≤25% tumour volume, which has been demonstrated to be a positive prognostic factor in different registries. I would encourage inclusion of patients with ≤25% tumour volume AND/OR ≤5 tumours. The success of the CtE in replicating the results of Hickey and Kennedy should be highlighted and their papers should be referenced in the review (data below). Collectively, these data strengthen the recommendations, which are consistent across three registries, and apply equally to resin and glass Y-90 microspheres. **Multicenter evaluation of the safety and efficacy of radioembolization in patients with unresectable colorectal liver metastases selected as candidates for ^{90}Y resin microspheres** Andrew S. Kennedy[1,2], David Ball[3], Steven J. Cohen[4], Michael Cohn[5], Douglas M. Coldwell[6], Alain Drooz[7], Eduardo Ehrenwald[8], Samir Kanani[9], Steven C. Rose[3], Charles W. Nutting[10], Fred M. Moeslein[11], Michael A. Savin[12], Sabine Schirm[1], Samuel G. Putnam III[13], Navesh K. Sharma[14], Eric A. Wang[15] • 606 patients, 11 institutions • Median survival: **2nd line 13 months** (10.5-14.6) **3rd line 9.0 months** (7.8-11.0) **≥4th line 8.1 months** (6.4-9.3) • Positive prognostic factors: ECOG 0 *v* ≥1 (p=0.009), disease stage (tumour volume, extrahepatic disease), liver function, leucocytes, prior chemotherapy A Kennedy *et al. J Gastrointest Oncol* 2015;6(2):134-42.	See above Studies from Hickey (2016) and Kennedy (2015) were considered as part of the evidence review and development of the draft policy proposition.	No action required.

	 The 3 SIRT products currently available are viewed by NICE as minor modifications of the same treatment and not separate technologies. All 3 products have the same indications for use and the same mode of action. Product selection should be at the discretion of the clinical team, as there are dosing advantages depending on the different Yttrium-90 and Holmium-166 products used. The CtE data reports resin use in 86% and glass in 14%, but never intended to compare different technologies. There are technical advantages to each product, which will benefit patients. Instead of being restricted to Y-90 resin microspheres, the commissioning should offer any SIRT product shown to be safe and effective, which ensures patient access to the optimal treatment technology determined by the treating clinical team. *Recommendation for 6 week public consultation.*	Noted see above	