

Briefing Paper


Split Liver Variance

OPTN Liver and Intestinal Transplantation Committee

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Split Liver Variance

<i>Affected Policies:</i>	<i>9.11 Variances</i>
<i>Sponsoring Committee:</i>	<i>Liver and Intestinal Transplantation Committee</i>
<i>Public Comment Period:</i>	<i>January 22, 2019 – March 22, 2019</i>
<i>Board of Director's Date:</i>	<i>June 10-11, 2019</i>

Executive Summary

This proposal will create a variance to permit participating liver programs to split a liver and transplant the first segment into the candidate to whom it was allocated, and then transplant the remaining segment into another candidate at the same transplant hospital or an affiliated hospital after offering the remaining segment to the most urgent candidates within 500 nautical miles of the donor hospital. The goal is to increase the number of livers that are split and thereby increase the number of liver transplants available from the same donor pool. It aims to reduce the logistical and technical challenges currently associated with splitting a liver. The variance would be used to determine whether this change will in fact increase the number of transplants by increasing the number of livers that are split.

This variance was initially proposed by transplant hospitals and OPOs in region eight, who requested it as a regional variance. However, transplant hospitals in other regions expressed interest, and the Liver and Intestinal Transplantation Committee (Committee) proposes that this be an open variance that any liver transplant program can join.

What problem will this proposal address?

As of April 30, 2019, there are 13,262 liver candidates listed and awaiting transplant.¹ In 2018, there were 8,874 liver donors.² Because there are not enough livers donated to meet the demand for liver transplantation, 1,157 candidates died while awaiting liver transplant in 2018.³ Part of the OPTN Strategic Plan for 2018-2021 is to increase the number of transplants.⁴

One way to increase the number of transplants is to split livers. Split liver transplantation (SLT) increases the number of transplants from the same donor pool by “creating two partial grafts from one donor organ which can be given to two recipients”.⁵ The OPTN match run identifies a donor liver as having the potential to be split if all of the following criteria are met:

1. Donor is less than 40 years old
2. Donor is on a single vasopressor or less
3. Donor transaminases are no greater than three times the normal level
4. Donor mass index (BMI) is 28 or less.^{6,7}

¹ OPTN data. <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data> (Accessed April 30, 2019)

² There were 401 living liver donors and 8,473 deceased liver donors in 2018. OPTN data. <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data> (Accessed April 30, 2019)

³ OPTN data. <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data> (Accessed April 30, 2019)

⁴ The OPTN Strategic Plan is a roadmap to help prioritize major initiatives of the OPTN over a three-year period. It was approved by the OPTN Board of Directors in June 2018. OPTN Strategic Plan 2018-2021.

https://optn.transplant.hrsa.gov/media/2546/optn_unos_strategic_plan.pdf (Accessed December 14, 2018)

⁵ Jason Wertheim, Henrik Petrowsky, Sammy Saab, Jerzy Kupiec-Weglinski, and Ronald Busittil, “Major Challenges Limiting Liver Transplantation in the United States”, *Am J Transplant*, 2011 Sep; 11(9): 1773-1784

⁶ OPTN Policy 9.6.A: Segmental Transplant and Allocation of Liver Segments.

https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf (Accessed January 17, 2019)

⁷ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

More than 10% of all deceased donors meet these criteria, but less than 1.5% of donor livers have been split since the adoption of these criteria in 2010.⁸

However, there are challenges specific to SLT. The recovery and the transplant are both more complex procedures than recovery and transplantation of a whole liver, requiring detailed knowledge of liver anatomy and expertise in hepatobiliary surgery.⁹ Not all transplant hospitals have the expertise or willingness to perform SLT. In 2017, only 54 of the 147 active liver programs performed any SLT.¹⁰ There are additional challenges in coordinating SLT when two different surgical teams are involved and the recipients are at different transplant hospitals.

Livers are split both in situ and ex vivo. In situ splitting can increase intraoperative time and increase the risk of impacting extrahepatic organ retrieval teams or causing the donor to become hemodynamically compromised.¹¹ Case coordination is further complicated when the intended recipients are at two different hospitals. It is likely that the transplant teams from both hospitals will want to participate in the recovery¹², which can delay the donor recovery time and increase the amount of time required for the recovery procedure. When splitting occurs ex vivo in a recipient's hospital and the other graft must be transported to a secondary transplant hospital, it adds cold ischemic time for the second segment.¹³ In addition to recovery and transportation logistics, there are clinical decisions that must be coordinated between the two transplant teams, such as who has priority in deciding the splitting technique and how the blood supply and bile duct will be shared, as well as a backup plan in the event that the SLT is aborted late in the process.¹⁴ Although these decisions are most often made by the transplant team for the initial candidate, the ideal technique for the initial candidate may not be the best technique for ensuring that both segments have the best outcomes.¹⁵

Why should you support this proposal?

This proposal is a variance to investigate whether allowing a transplant hospital to transplant the second transplantable segment of a split liver into another potential recipient registered at the same transplant hospital or an affiliated hospital will incentivize splitting livers and increase the number of candidates transplanted with the same number of deceased donor livers. If the Committee's hypothesis is correct, this will increase the number of liver transplants and net survival for waitlisted candidates.¹⁶

How was this proposal developed?

SLT is typically performed by splitting a whole liver into a left-lateral segment and a right tri-segment.^{17,18} The left lateral segment is smaller, and typically transplanted into pediatric candidates and the larger right tri-segment is typically transplanted into an adult or larger pediatric candidate. It is less commonly split into right hemiliver and left hemiliver.¹⁹

⁸ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

⁹ Wertheim, et al., "Major Challenges Limiting Liver Transplantation in the United States".

¹⁰ This is approximately 1/3 of the 143 active liver programs during the same year. Based on OPTN data as of December 7, 2018.

¹¹ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

¹² OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

¹³ Wertheim, et al., "Major Challenges Limiting Liver Transplantation in the United States".

¹⁴ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

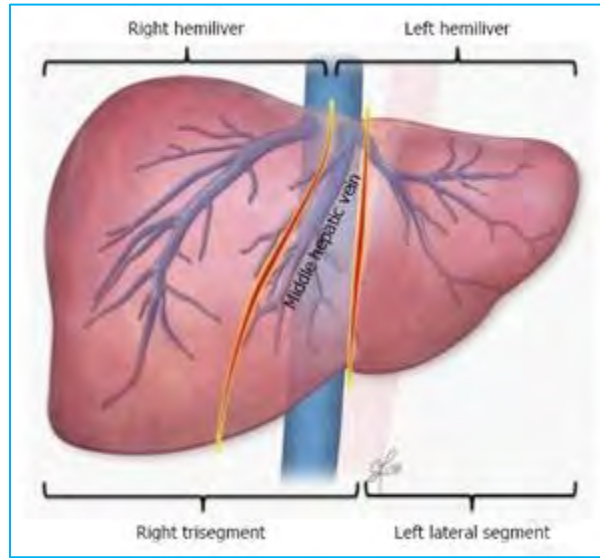
¹⁵ Koji Hashimoto, Mastato Fujiki, Cristiano Quintini, Federico Aucejo, Teresa Diago Uso, Dymrna Keey, Bijan Egtesad, John Fung, Charles Miller, "Split Liver Transplantation in Adults", *World J Gastroenterol*, 2016 Sep 7; 22(33): 7500-7506.

¹⁶ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

¹⁷ Wertheim, et al., "Major Challenges Limiting Liver Transplantation in the United States".

¹⁸ Hashimoto, et al., "Split Liver Transplantation in Adults".

¹⁹ Splitting the liver into right tri-segment and left lateral segment allows for avoiding multiple small branches and reduces the surgical complexity compared to splitting into hemi-liver segments. Hashimoto, et al., "Split Liver Transplantation in Adults".

Figure 1: Graft types for SLT²⁰

There is an existing open variance under which participating centers can choose to split a liver and utilize either the right lobe (right hemiliver) or the right tri-segment in the patient to whom that liver was allocated and then use the left hemiliver or the left lateral segment for another candidate at the same center or an affiliated pediatric center.²¹ The Committee reviewed data on the existing variance at its meeting on March 29, 2018.²² There are currently four OPOs and one region participating in the existing variance. Only four of the split liver transplants performed between the 2010 implementation of the variance and December 31, 2017 appear to have been allocated using the existing open variance.²³

The purpose of the existing split liver variance was to incentivize SLT when livers are initially allocated to adult candidates, in order to create more left lateral segments for pediatric transplants. Since there have only been four transplants that meet the variance requirements at participating transplant programs in over seven years²⁴, any impact on this goal as a direct result of variance participation has been minimal. Part of the reason for this may be that initial results showed SLT using the right tri-segment had an increased risk of morbidity and mortality in adult recipients.²⁵ When risk factors, including longer ischemic

²⁰ Hashimoto, et al., "Split Liver Transplantation in Adults".

²¹ *Proposed Committee-Sponsored Alternative Allocation System (CAS) for Split Liver Allocation*, OPTN Liver and Intestinal Organ Transplantation Committee, December 2018. OPTN Policy 9.11.A: Open Variance for Segmental Liver Transplantation (approved but not yet implemented). "Under this variance, a transplant program may offer the remaining left lobe or left-lateral segment into a different, medically suitable, potential recipient registered at the same transplant hospital or an affiliated pediatric institution instead of offering the remaining segment to potential recipients at other transplant programs. The transplant program must determine potential recipient for the second segment by using the same match run used to allocate the right lobe or tri-segment. Additionally, the transplant program must document all refusals of potential transplant recipients that are prioritized ahead of the potential transplant recipient that received the second segment."

OPTN Policy 9.9.A: Open Variance for Segmental Liver Transplantation.
https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf (Accessed January 17, 2019).

²² Meeting Summary for March 29, 2018 meeting, OPTN Liver and Intestinal Organ Transplantation Committee, https://optn.transplant.hrsa.gov/media/2498/20180329_liver_meetingsummary.pdf (Accessed December 14, 2018).

²³ S. Noreen and T. Baker, Evaluation of Open Variance for Segmental Liver Transplantation, OPTN Liver and Intestinal Transplantation Committee Meeting, March 29, 2018.

²⁴ S. Noreen and T. Baker, Evaluation of Open Variance for Segmental Liver Transplantation, OPTN Liver and Intestinal Transplantation Committee Meeting, March 29, 2018.

²⁵ Hashimoto, et al., "Split Liver Transplantation in Adults". J. Emond, P. Whittington, J. Thistlethwaite, D. Cherqui, E. Alonso, I. Woodle, P. Vogelbach, S. Busse-Henry, A. Tucker, and C. Broelsch, *Transplantation of Two Patients with One Liver: Analysis of a Preliminary Experience with "Split Liver" Grafting*, *Ann Surg.*, 1990, Jul; 212(1): 14-22. C.

times, are avoided, right tri-segments are no longer considered marginal by experienced programs.²⁶ The Committee hypothesized that a transplant program would be more likely to perform SLTs if it was able to primarily transplant the left segment and also use the remaining right segment at their program, as data supports better outcomes associated with right tri-segments. This was consistent with the recommendation in the 2016 white paper published by the OPTN supporting consideration of a change in allocation policy to facilitate SLT so that the left-lateral segment or extended right lobe is allocated to the first candidate and the remaining liver segment is allocated to a second candidate.²⁷

A member of the Committee championed the idea that allowing both segments of split livers to be transplanted at the same center, regardless of which segment was transplanted in the first recipient, would increase split liver transplantation²⁸, and gathered support from others to test the idea with a variance in region eight. Transplant hospitals and OPOs in region eight unanimously agreed in early 2018 to request a variance for the transplantation of split livers that would allow participating programs more opportunities to transplant both segments at the same center.

The variance as proposed would permit participating transplant hospitals to split a liver and use any segment of the liver for the patient for whom the liver was accepted and then use the remaining segment for another candidate at their center or an affiliated hospital after it was offered to candidates on the match run classifications for Status 1 or with a model for end-stage liver disease (MELD) or pediatric end-stage liver disease (PELD) score of 33 or higher at liver transplant programs within 500 nautical miles (NM) of the donor hospital.

The Committee discussed the scope of the variance and whether this should be an open or closed variance. An open variance permits members across the country who meet the requirements to apply and join the variance.²⁹ A closed variance contains specific limitations for participation and does not allow other members to apply to join it. The variance as originally proposed by region eight was a closed variance that only applied to members in region eight. At the December 3, 2018 OPTN Board of Directors (Board) meeting, an amendment to the proposed policy to “Eliminate the use of DSAs and Regions in Liver Allocation” was offered by a member of the Board.³⁰ The amendment would have created an open variance that would have allowed any participating liver transplant hospital to split an allocated liver, and transplant the first liver segment into the candidate to whom the organ was allocated, while transplanting the second liver segment to a candidate registered at the same transplant program. After some discussion by the Board, the amendment was voluntarily withdrawn by the sponsor with a request that the Committee consider broadening the concept of a variance for region eight to permit other members to join. Following the Board meeting, the Committee discussed this scope and agreed that the variance should be released for public comment as an open variance.

The proposal was circulated for public comment as an open variance, with feedback requested on whether it should be open or closed and whether members would be interested in participating in the variance.

Broelsch, J. Emond, P. Wittington, J. Thistlethwaite, A. Baker, and J. Lichor, *Application of Reduced-Size Liver Transplants as Split Grafts, Auxiliary Orthotopic Grafts, and Living Related Segmental Transplants*, *Ann Surg.*, 1990 Sep; 212(3): 368-377.

²⁶ Hashimoto, et al., “Split Liver Transplantation in Adults”. V. Corno, M. Colledan, M. Dezza, M. Guizzetti, A. Lucianetti, G. Maldini, D. Pinelli, M. Giovanelli, M. Zambelli, G. Torre, et al. “Extended Right Split Liver Graft for Primary Transplantation in Children and Adults”, *Transpl Int.* 2006;19:492–499. V. Corno, M. Colledan, M. Dezza, M. Guizzetti, A. Lucianetti, G. Maldini, D. Pinelli, M. Giovanelli, M. Zambelli, G. Torre, et al. “Extended Right Split Liver Graft for Primary Transplantation in Children and Adults”, *Transpl Int.* 2006;19:492–499.

²⁷ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

²⁸ “More widespread use of split liver transplantation could be encouraged by allocating both liver segments to the same transplant center.” Leigh Anne Dageforde and William Chapman, “Split Liver Grafts Can Benefit Both Pediatric and Adult Liver Transplants Recipients and Programs”, *Pediatric Transplant*, 2017; 21: e12934.

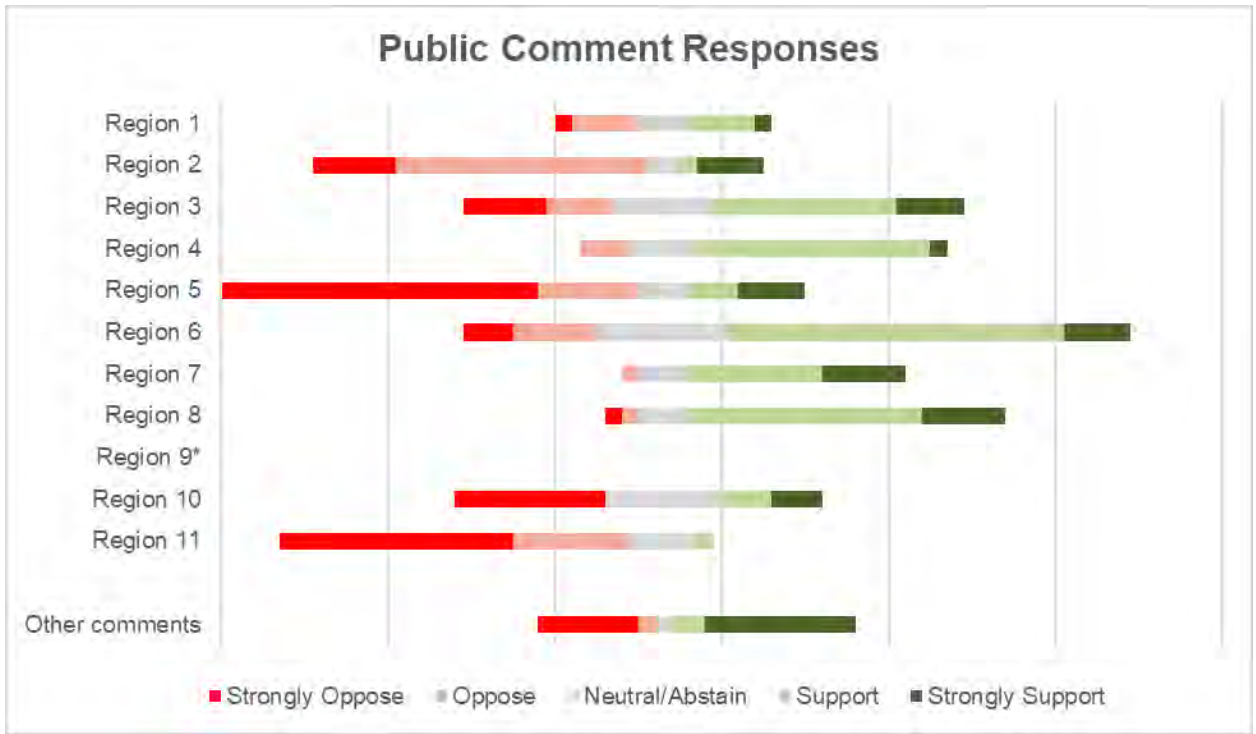
²⁹ Compare OPTN Policy 1.1 “Closed Variance” and “Open Variance.” OPTN Policy 15.7: *Open Variance for the Recovery and Transplantation of Organs from HIV Positive Donors* is an example of an open variance.

³⁰ OPTN Board of Directors Meeting Transcript, Dallas, TX, December 3-4, 2018.

https://optn.transplant.hrsa.gov/media/2767/board_liver_discussion_transcript_201812.pdf (Accessed December 21, 2018).

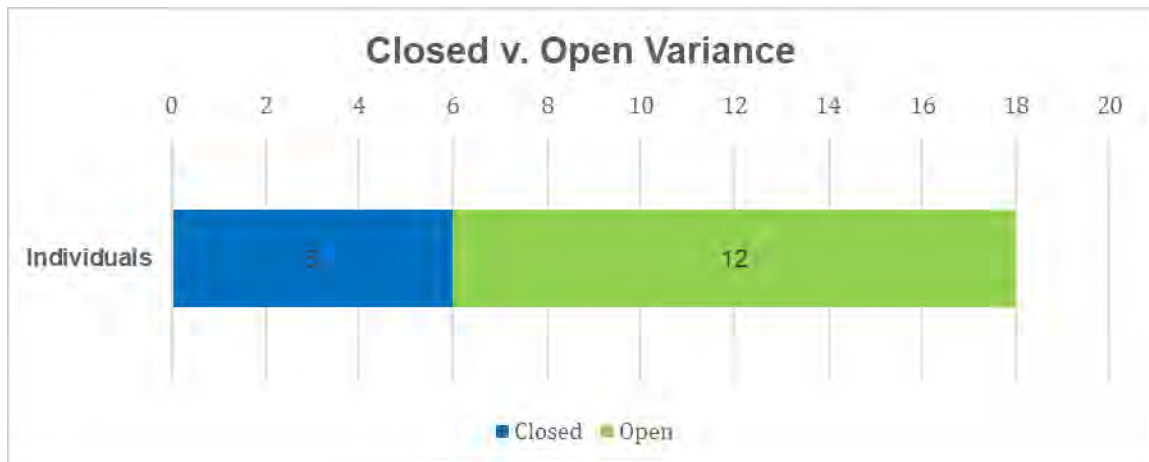
There was mixed support for the variance as proposed.

Figure 2: Public comment responses



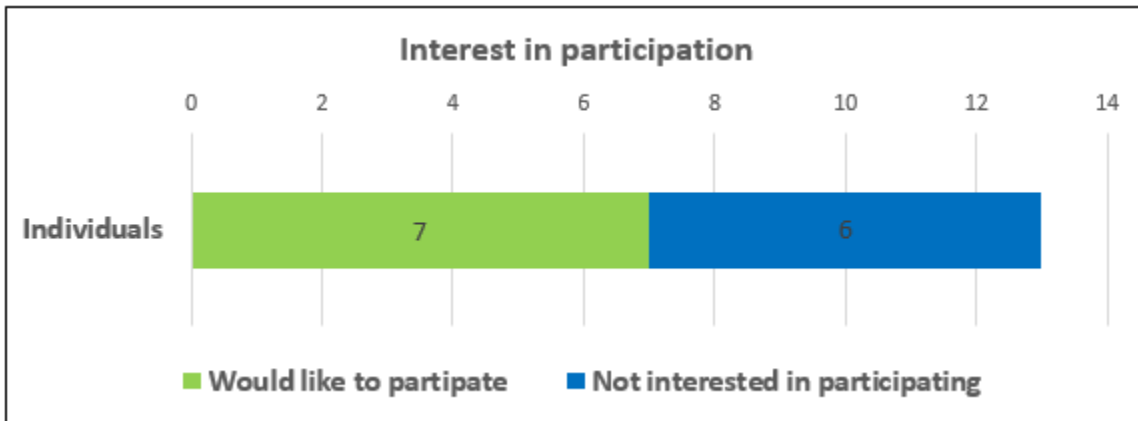
There were also mixed responses regarding whether to offer this as an open or closed variance, with most support for an open variance.

Figure 3: Public comment responses regarding whether variance should be open or closed



As part of their formal comment, region seven specifically expressed interest in participating in the variance. Some members of other regions also expressed interest.

Figure 4: Public comment responses regarding whether the respondent was interested in participating in the variance



Transplant societies also had mixed opinions on the proposal. The American Society for Transplantation (AST) could not come to clear agreement within its membership to either support or oppose the variance. Pediatric members supported the variance, but also noted that there are other reasons why split livers are underutilized. The pediatric members advocated for developing an allocation system that mandates splitting of livers that meet certain criteria. Other members of the AST felt that the remaining segment of the liver should be offered to Status 1 candidates and candidates with a MELD greater than 32 prior to recovery, but if the segment is not accepted prior to recovery, then the primary program should be allowed to allocate the segment to a candidate at their program. On the other hand, some members proposed that the remaining segment should not need to return to the match run at all. And finally, the AST recommended that the outcomes of split liver transplantation be monitored separately from total deceased donor outcomes, so as to no disincentivize programs from splitting livers.

The American Society of Transplant Surgeons (ASTS) supported the variance but closed to region eight. The American Society for Histocompatibility and Immunogenetics (ASHI) and the Society for Pediatric Liver Transplantation (SPLIT) supported the variance as proposed. The Association of Organ Procurement Organizations (AOPO) supported the variance as long as it does not negatively impact the availability of left lateral segments for pediatric candidates and it is monitored to ensure that livers are being accepted for and transplanted into the appropriate candidates.

Based on the public comment preference for an open variance, and the desire of other transplant programs to participate, the Committee is proposing that this variance be an open variance, as proposed in public comment. Any liver transplant program in the country will be eligible to apply.

Variance Requirements

OPTN Policy requires that proposed variances include:

1. The purpose for the proposed variance and how the variance will further this purpose.
2. If a member's application to create, amend, or join a variance will require other members to join the variance, the applicant must solicit their support. Committees will not review a member's variance application unless the applicant receives affirmative support from at least 75% of the members required to join the proposed variance.
3. A defined expiration date or period of time when the variance will end, the participating members will report results, and the sponsoring Committee will evaluate the impact of the variance.
4. An evaluation plan with objective criteria to measure the variance's success achieving the variance's stated purpose.

5. Any anticipated difficulties in demonstrating whether the variance is achieving its stated purpose.
6. Whether this is an open variance or closed variance and, if this is an open variance, any additional conditions for members to join this variance³¹

1. Purpose

The purpose of this variance is to encourage SLT, as discussed further below in *How well does this proposal address the problem statement?*

2. Member Support

The members of region eight specifically asked for the creation of this variance. All of the liver transplant hospitals and OPOs in region eight expressed their affirmative support for the variance to apply to region eight. Since all of the liver transplant programs of region eight agreed, that constituted more than the required 75% of transplant programs who would have been required to join in the variance as they proposed it. After the Committee received the letter of support from the members in the region, the Committee reviewed the variance application and also considered the possibility of creating an open variance, which would allow other OPTN members to apply to participate.

A liver transplant program may join the variance alone, or in conjunction with an affiliated liver transplant program. The variance will require that when members are affiliated for purposes of the variance, both affiliated transplant programs must apply to participate. One member will not be permitted to require the participation of an affiliated program without its agreement.

3. Time Limited

The variance is proposed to expire three years after implementation. Based on the evaluation of the variance, the Committee will then either recommend that the variance be modified, terminated, replaced with a national policy, or extended to collect more data.

4. Evaluation

The Committee's plan for evaluating the impact of the variance is outlined below under: *How will the sponsoring Committee evaluate whether this proposal was successful post implementation?*

5. Anticipated Difficulties

The Committee recognizes that not all donors or candidates are good candidates for SLT.³² Even if there are behavior changes as a result of the variance, the increase in SLT will likely be small.

There is not a list of affiliated programs already in the OPTN computer system. In order to track which programs are affiliated, participating transplant programs will have to self-identify these affiliations.

OPOs will have two sets of rules for allocation of split livers – one set for when the liver is split by a participating transplant program, and another for the programs that are not participating in this variance. In order to clearly track the outcomes of this variance, bypassed candidates will have to be coded in a specific way. It may be difficult for OPOs to track which hospitals are participating in the variance, and ensure that staff are trained on the differences and when to follow which rules. The Committee plans to develop resources for OPOs to help with this anticipated difficulty.

³¹ OPTN Policy 1.3.B: Application for a Variance

³² Visual and manual examination of the liver during recovery, as well as consideration of factors such as a low platelet counts, history of heavy alcohol use, or age of younger donors are essential in SLT. Hashimoto, et al., "Split Liver Transplantation in Adults".

6. Conditions

This will be an open variance. Members that wish to participate in the variance must have an approved liver transplant program and submit an application to the OPTN. If they wish to share with an affiliated transplant hospital, both hospitals must participate in the variance, and one of the affiliated transplant hospitals must have a pediatric liver transplant program component.

How well does this proposal address the problem statement?

Since 2011, there have been between 61 and 89 livers split each year, in which the majority of the time, the primary recipient was a pediatric candidate and the secondary recipient was an adult (Table 1). Only four of these transplants were potentially under the existing variance.³³

Table 1: SLT Events in the U.S. 12/2/2010-12/31/2017³⁴

Age of Primary Recipient	Age of Secondary Recipient	All		2010		2011		2012		2013		2014		2015		2016		2017	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Pediatric	Pediatric	41	8.6	1	12.5	6	10.0	8	13.1	8	11.6	4	6.7	2	3.6	4	4.9	8	9.6
	Adult	438	91.4	7	87.5	54	90.0	53	86.9	61	88.4	56	93.3	54	96.4	78	95.1	75	90.4
	Total	479	100.0	8	100.0	60	100.0	61	100.0	69	100.0	60	100.0	56	100.0	82	100.0	83	100.0
Adult	Pediatric	10	27.0	1	100.0	2	33.3	1	20.0	4	66.7	0	0.0	1	20.0	1	16.7	0	0.0
	Adult	27	73.0	0	0.0	4	66.7	4	80.0	2	33.3	3	100.0	4	80.0	5	83.3	5	100.0
	Total	37	100.0	1	100.0	6	100.0	5	100.0	6	100.0	3	100.0	5	100.0	6	100.0	5	100.0

The Committee posits that this is because a transplant hospital that initially receives the liver offer for an adult candidate who would be appropriate to transplant with the right tri-segment may not be as likely to have a pediatric candidate who would benefit from the left lateral segment.³⁵ The Committee proposes a new variance to test the theory that reducing the difficulty of coordinating two transplant hospitals with two transplant teams will achieve better efficiency in the placement of SLT organs, increase the frequency of SLT and thereby increase the number of transplanted organs and net survival.

By more explicitly permitting the transplant hospital that performs the split and transplants the first candidate to use the remaining segment³⁶ for another candidate at that hospital or an affiliated hospital, many of the difficulties associated with SLT are removed or reduced. This includes coordinating recovery times and deciding the type of split and division of blood vessels and bile duct since there is only one hospital involved, or in the case of affiliated hospitals, the two involved hospitals are physically close to one another and already have an established working relationship.

The proposed variance requires the second segment be offered to candidates with Status 1A or 1B and MELD/PELD scores of 33 and higher at transplant programs within 500 NM of the donor hospital before they are used for a candidate at the initial transplant hospital.³⁷ This will ensure that candidates who are

³³ The Committee reviewed data based on SLT that were performed at the same hospital, participating in the variance, with the right tri-segment or right lobe transplanted into the first candidate. There was no identifier to know for sure that the variance was being used in these cases. S. Noreen and T. Baker, Evaluation of Open Variance for Segmental Liver Transplantation, OPTN Liver and Intestinal Transplantation Committee Meeting, March 29, 2018.

³⁴ S. Noreen and T. Baker, Evaluation of Open Variance for Segmental Liver Transplantation, OPTN Liver and Intestinal Transplantation Committee Meeting, March 29, 2018.

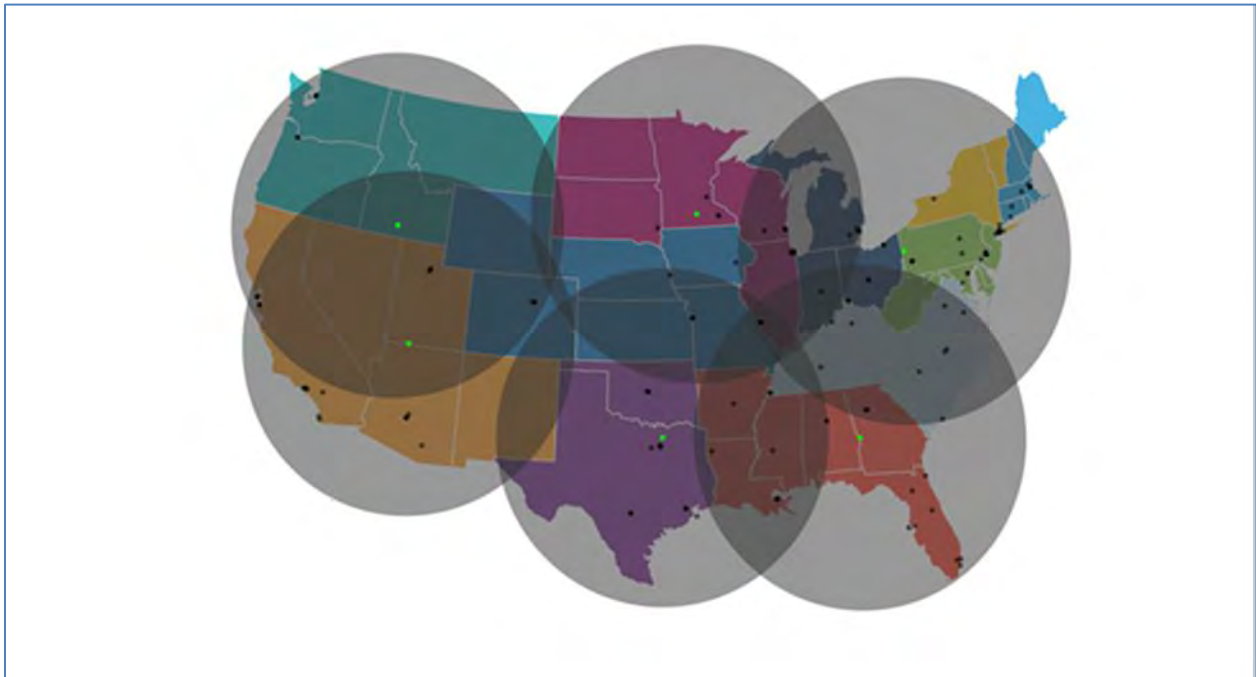
³⁵ As of December 14, 2018, there are 433 pediatric candidate on the liver transplant waitlist and 13,118 adult candidates. OPTN data. <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/> (Accessed December 14, 2018).

³⁶ This would be different from the current default allocation rules, under which the full liver is offered according to the match run for that organ, and the surgeon for the candidate that accepts the organ has the option to split the liver. If it is split, the remaining segment must also be offered according to the match run. OPTN Policy 5.9 Released Organs. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf. (Accessed December 22, 2018).

³⁷ In the case of blood type O donors, offers are only required to be made to blood type O and B candidates with status 1 or MELD of at least 33 within 500 NM of the donor hospital. Because blood type A and AB candidates are

most medically urgent receive offers for the remaining graft. Without this provision to offer the liver segment to the most medically urgent candidates before the segment is offered to other candidates at the same center, the Committee was concerned that the variance could disadvantage patients by reducing access to offers where hospitals are already splitting livers within the distribution area. For instance, if there is a donor at a hospital in Pittsburgh, Pennsylvania and the liver is accepted for a candidate at a hospital in Chicago, Illinois, then the second candidate at the Chicago hospital would have access to the offer of the remaining segment before medically urgent candidates listed at hospitals that may not be participating in the variance, but are all within 500 NM of the donor hospital.

Figure 5: Demonstration of 500 NM Radius Circles around Donor Hospitals



The question of whether to allow a transplant hospital to use both segments of a divided organ was also considered by the OPTN Kidney Transplantation Committee (Kidney Committee) when developing the proposal for *Improving Allocation of En Bloc Kidneys* in 2017.³⁸ For kidneys that are initially allocated *en bloc*, but then split, the second organ must be allocated according to the match run, and there is no exception allowing them to be used at the same transplant hospital.³⁹ However, this is distinguishable from split livers because the kidneys that qualify to be offered *en bloc* are smaller and more marginal and less likely to be used for transplant if they are used alone, so the increase in transplants that can be gained from *en bloc* allocation is more likely to result from the initial *en bloc* allocation instead of the split.⁴⁰

deprioritized in the allocation of livers from O donors, offers to these candidates will not be required for these segments.

³⁸ *Improving Allocation of En Bloc Kidneys*, OPTN Kidney Transplant Committee, December 2017, https://optn.transplant.hrsa.gov/media/2327/kidney_boardreport_enbloc_201712.pdf (Accessed December 27, 2018).

³⁹ *Improving Allocation of En Bloc Kidneys*, OPTN Kidney Transplant Committee, December 2017, pages 11-14.

⁴⁰ *Improving Allocation of En Bloc Kidneys*, OPTN Kidney Transplant Committee.

Was this proposal changed in response to public comment?

In the public comment feedback, some commenters and regional meeting attendees were concerned that the variance would unfairly benefit candidates at pediatric programs over adult programs. There were suggested amendments from multiple regions to limit the types of split that would be allowed in order to ensure that the variance incentivizes splitting additional organs instead of simply changing sharing patterns for the SLT already occurring. There were concerns about members potentially artificially creating smaller distribution areas simply by affiliating with several strategically chosen programs.

In response, the Committee narrowed the scope of affiliations that are permitted under the variance. If a program desires to have the second segment transplanted at an affiliated transplant program, they must identify that program ahead of time. Further, each program may only have a single affiliation for purposes of the variance, and one of the affiliated programs must have a pediatric liver component. Both of the affiliated programs must be members of the variance.

The structure and language of the proposed policy was also changed in response to concerns during public comment about the clarity and specificity of the proposed policy language. These changes did not impact the substance of the variance, but are intended to ensure that the policy language is as clearly and accurately written as possible.

Which populations are impacted by this proposal?

This proposal aims to increase the number of transplants and provide greater net survival by decreasing time on the waiting list and therefore waiting list mortality.⁴¹ As most commonly performed, SLT involves the division of a donor liver from a deceased adult, and transplantation of one segment into an adult candidate and another into a pediatric candidate.⁴² Therefore, if more livers are split, the expectation is that it will increase the number of split livers transplanted into both adult and pediatric candidates. SLT may be appropriate for smaller adult candidates who may not be able to accept a whole liver from a larger donor⁴³, but may be able to use a segment that may be too small for larger candidates⁴⁴. For this reason, it may improve access for small women who are currently disadvantaged in liver allocation⁴⁵.

It is unknown specifically how many more livers will be split under this variance, and therefore how many additional transplants will be performed. The recovery and the transplant are both more complex procedures than recovery and transplantation of a whole liver.⁴⁶ The changes as a result of the variance will be analyzed by the Committee on an ongoing basis to evaluate the effectiveness and impact of the variance as discussed below in the section, *How will the sponsoring Committee evaluate whether this proposal was successful post implementation?*

⁴¹ OPTN Split Versus Whole Liver Transplantation, OPTN Ethic Committee, December 2016, <https://optn.transplant.hrsa.gov/resources/ethics/split-versus-whole-liver-transplantation/> (Accessed December 14, 2018).

⁴² Jonathan Roach, "Split Liver Transplantation", *MedScape*, January 18, 2017.

<https://emedicine.medscape.com/article/1014235-overview> (Accessed December 14, 2018).

⁴³ Alina Allen, Julie Heimbach, Joseph Larson, Kristin Mara, W. Kim, Patrick Kamath, Terry Therneau, "Reduced Access to Liver Transplantation in Women: Role of Height, MELD Exception Scores, and Renal Function Underestimation", *Transplantation*: October 2018 - Volume 102 - Issue 10 - p 1710–1716, doi: 10.1097/TP.0000000000002196.

⁴⁴ Roach, "Split Liver Transplantation".

⁴⁵ Allen, et al., "Reduced Access to Liver Transplantation in Women: Role of Height, MELD Exception Scores, and Renal Function Underestimation".

⁴⁶ Wertheim, et al., "Major Challenges Limiting Liver Transplantation in the United States".

How does this proposal comply with the Final Rule?

All variances must meet the requirements contained in OPTN Policy⁴⁷ and the Final Rule⁴⁸. The Final Rule requires variances to be accompanied by a research method, include data collection and analysis plans, and be time limited.⁴⁹ The Final Rule also requires that variances with the goal of improving allocation must be developed “in accordance with §121.4”, which in turn incorporates the requirements in §121.8 that allocation policies “(1) Shall be based on sound medical judgment; (2) Shall seek to achieve the best use of donated organs; (3) Shall preserve the ability of a transplant program to decline an offer of an organ or not to use the organ for the potential recipient in accordance with §121.7(b)(4)(d) and (e); (4) Shall be specific for each organ type or combination of organ types to be transplanted into a transplant candidate; (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;...(8) Shall not be based on the candidate's place of residence or place of listing, except to the extent required by paragraphs (a)(1)-(5) of this section.” This proposal meets the requirements of the Final Rule.

- **Shall be based on sound medical judgment:** The Committee proposes the variance based on sound medical judgment, including literature that supports potential positive outcomes from SLT for more candidates than are currently transplanted as SLT.⁵⁰ Some of the challenges of SLT can be reduced when both segments are transplanted at the same program, or closely affiliated programs.⁵¹ The variance is being used to test the theory that permitting more segments to remain at the same program will increase SLT, and the outcomes from the variance will be carefully considered to inform whether this approach should become policy for the nation.
- **Shall seek to achieve the best use of donated organs:** The Committee believes that maximizing the gift of organ donation by using each donated organ to its full potential achieves the best use of donated organs. This variance seeks to achieve the best use of donated organs by encouraging SLT, which will result in two transplants from one donated organ.
- **Shall be designed to avoid wasting organs:** Under the current policy, it is possible that partial livers are being used and the remaining segment is not being transplanted.⁵² This is viewed by the Committee as an example of organ wastage. The variance is designed to avoid wasting organs by encouraging the transplantation of both liver segments.
- **Shall be designed to avoid...futile transplants:** A futile transplant may occur if a recipient is transplanted with an organ that does not continue to function soon after transplantation. This proposed variance does not incentivize futile transplants. Transplantation of both segments of a liver can result in successful post-transplant outcomes.⁵³
- **Shall be designed to...promote patient access to transplantation:** This proposal promotes liver candidate access to transplants by increasing the total overall number of livers available for transplant. Additionally, this proposal is likely to result in better pediatric patient access to liver transplantation, because when a liver is split, at least one of the segments is typically used for a pediatric patient.⁵⁴
- **Shall be designed to...promote the efficient management of organ placement:** A proposal that reduces logistical complications associated with procuring an organ and transporting it from the donor to the candidate promotes efficient management of organ placement. This proposed variance promotes the efficient management of organ placement by reducing the transportation and coordination required in SLT cases by more specifically detailing when a transplant program

⁴⁷ OPTN Policy 1.3 Variances

⁴⁸ 42 C.F.R. § 121.8(g)

⁴⁹ 42 C.F.R. § 121.8(g)

⁵⁰ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

⁵¹ Wertheim, et al., “Major Challenges Limiting Liver Transplantation in the United States”.

⁵² OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

⁵³ Hashimoto, et al., “Split Liver Transplantation in Adults”. V. Corno, et al. “Extended Right Split Liver Graft for Primary Transplantation in Children and Adults”. U. Maggi, et al., “Fifteen Years and 382 Extended Right Grafts from *in situ* Split Livers in a Multicenter Study: Are These Still Extended Criteria Liver Grafts?”

⁵⁴ V. Corno, et al. “Extended Right Split Liver Graft for Primary Transplantation in Children and Adults”.

can allocate the remaining segment to a candidate at the same transplant program or affiliated programs.

- **Shall not be based on the candidate's place of residence or place of listing, except to the extent required [by the aforementioned criteria]:** A proposed variance may be based on a candidate's residence or place of listing only to the extent required to achieve the considerations listed above. This proposed variance considers geography with regard to the distribution of the remaining segment. The Committee proposes allocating the remaining segment to the most urgent candidates within 500 NM of the donor hospital before allocating directly to a candidate at the same program or affiliated program. The Committee decided to limit the allocation of the remaining segment to these proximate, urgent candidates in order to achieve the goals stated above, particularly making best use of donated organs, avoiding organ wastage, promoting access to transplantation, and efficient management of organ placement. The Committee determined that the liver is more likely to be split if the remaining segment will be transplanted by the transplant program that is performing the split⁵⁵, therefore limiting the distance through which the remaining segment is offered is necessary to achieve the best use of donated organs as well as to avoid organ wastage. Likewise, as this would result in more SLTs, limiting the distance through which the remaining segment is offered will promote patient, particularly pediatric and small adult patient, access to transplantation.⁵⁶ Finally, it would be inefficient to require the remaining segment to be offered according to the entire match run. It is difficult to find candidates to accept the remaining segment⁵⁷, and requiring an exhaustion of the match run would likely result in more organ wastage, as a candidate would be less likely to be identified while the organ was still viable. The time required to do so, as well as the time required to transport the remaining segment from the donor to that candidate, would also likely result in more organ wastage, as there may be too much cold ischemic time on the organ at the point that it makes it to its final destination.⁵⁸

This proposed variance is not otherwise based on a candidate's place of residence or place of listing. A transplant program can determine whether it wishes to join the variance, and there is no geographic restriction for programs that wish to join.

Although the framework variations outlined in this briefing paper address certain aspects of the Final Rule listed above, Committee discussions did not demonstrate impacts on the following aspects of the Final Rule:

- Shall preserve the ability of a transplant program to decline an offer of an organ or not to use the organ for the potential recipient in accordance with §121.7(b)(4)(d) and (e);
- Shall be reviewed periodically and revised as appropriate;
- Shall include appropriate procedures to promote and review compliance including, to the extent appropriate, prospective and retrospective reviews of each transplant program's application of the policies to patients listed or proposed to be listed at the program.

How does this proposal impact the OPTN Strategic Plan?

1. *Increase the number of transplants:* The proposal is expected to increase the number of transplants by increasing the incentive to use a single liver to transplant two candidates.
2. *Improve equity in access to transplants:* This proposal may improve equity in access to transplant for smaller female candidates or pediatric candidates.

⁵⁵ OPTN Split Versus Whole Liver Transplantation, OPTN Ethics Committee.

⁵⁶ V. Corno, et al. "Extended Right Split Liver Graft for Primary Transplantation in Children and Adults."

⁵⁷ Wertheim, et al., "Major Challenges Limiting Liver Transplantation in the United States."

⁵⁸ V. Corno, et al. "Extended Right Split Liver Graft for Primary Transplantation in Children and Adults."

3. *Improve waitlisted patient, living donor, and transplant recipient outcomes:* There is no expected impact on this goal. However, the Committee will review the outcomes as part of the evaluation of the variance to ensure that it does not negatively impact recipient outcomes.
4. *Promote living donor and transplant recipient safety:* There is no impact to this goal.
5. *Promote the efficient management of the OPTN:* There is no impact to this goal.

What are the potential costs associated with this proposal?

Member

Minimal implementation effort at both OPO and Transplant Hospitals is estimated since many centers are already performing split liver transplants. Transplant costs are similar for either standard or split liver transplants.

If a liver is split, transportation cost may increase if each of the transplants is performed in a different hospital. Time in the operating room is always a variable that may affect cost as well.

Overall, this policy should increase the volume of transplants, with minimal additional cost.

Implementation time to educate staff is estimated at less than one month.

UNOS

Development and implementation effort associated with this proposal is minimal. Committee work and proposal writing managed by the Policy and Community Relations department is estimated at just under 100 hours. The Professional Education department will create a small instructional product to educate the community, while the communications will send policy notices, and other items to inform the community of the change.

How will the OPTN implement this proposal?

OPTN will provide information to interested members about how to apply to participate in the variance. OPTN will provide materials explaining the allocation process for split livers. OPTN will evaluate the variance, as detailed below in *How will the sponsoring Committee evaluate whether this proposal was successful post implementation?* The variance will expire three years after implementation.

This proposal will not require programming in UNetSM. However, the programming enhancements to UNet to ensure efficiency of placement are being considered.

How will members implement this proposal?

Transplant Hospitals

Transplant hospitals that wish to participate in the variance will have to submit an application to the OPTN to participate. If the transplant hospital wants to include an affiliated program in the variance, the affiliated program must be identified in the variance application and must also apply to participate in the variance. Applications will be accepted on a rolling basis.

Participating transplant hospitals will also have to communicate with OPO staff who are placing split livers to ensure that the OPO is familiar with the variance requirements.

Participants in the variance will be required to submit data to the Committee for review on an annual basis and at least 6 months prior to the expiration date of the variance.

OPOs

OPOs will need to be familiar with which transplant hospitals are participating in the variance, and will need to train staff on the differences in allocation when the variance is used. OPOs will need to report a specific bypass code for certain candidates when the variance is used.

Will this proposal require members to submit additional data?

Transplant programs that wish to participate will be required to submit an application to participate in the variance.

Participating transplant programs will be required to report the following information about each SLT performed or attempted under this variance by their program at 1 year, 2 years, 2.5 years and 3 years after the implementation of the variance:

1. Primary transplant recipient age, allocation MELD/PELD at transplant, and type of liver segment (left lobe, left lateral segment, right lobe, right tri-segment)
2. Secondary transplant recipient age, allocation MELD/PELD at transplant, and type of liver segment
3. Split liver transplant events for which the second liver segment was unable to be placed or transplanted
4. Split liver transplant events for which the second liver segment was accepted by another, non-affiliated transplant program

Data already routinely collected and the status reports will aid the Committee in determining if the variance achieved its stated purpose.

How will members be evaluated for compliance with this proposal?

The proposed language will not change the current routine monitoring of OPTN members. Any data submitted to the OPTN Contractor may be subject to review, and the OPTN Contractor will continue to review deceased donor match runs to ensure that allocation is carried out according to OPTN Policy. Members are required to provide documentation as requested.

How will the sponsoring Committee evaluate whether this proposal was successful post implementation?

This variance will be formally evaluated approximately 1 year, 2 years, and 2 and a half years post-implementation.

The following questions, and any others subsequently requested by the Committee, will guide the evaluation of the proposal after implementation:

- Has the number of split liver transplants increased?
- Have the characteristics of split liver recipients changed?
- Has there been a change in liver discards?
- If livers are split, did the remaining segment stay at the same or affiliated program?
- Has the number of programs performing split liver transplants increased?

The following metrics, and any others subsequently requested by the Committee, will be evaluated as data become available to compare performance before and after the implementation of this variance. These metrics will be reviewed for participating transplant programs, as well as compared between participating and non-participating programs as appropriate:

- The number (and percent) of liver transplants (whole vs. segment) overall, and by both recipient and donor demographics, including but not limited to:
 - Recipient age, allocation MELD/PELD or status at transplant, primary recipient liver segment (left lobe or left-lateral segment vs. right lobe or right tri-segment)
- Descriptive statistics on primary and secondary recipient of split liver, including but not limited to:
 - Allocation MELD/PELD at transplant, gender, OPTN region
- Geography of secondary recipient of liver segment as it relates to primary recipient
- The number (and percent) of deceased donor liver transplant programs performing split liver transplants

After this evaluation but prior to the variance's expiration date, the Committee will make a recommendation to the Board regarding whether to modify, terminate or extend the variance.

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

[Subsequent heading numbers, classifications, numbered lists, table captions, and any cross-references affected by the re-numbering of these policies will also be changed as necessary.]

1 **9.11.A Open Variance for Right Segmental Liver Transplantation**

2 **9.11.C Open Variance for Any Segment Liver Transplantation**

3 This is an open variance. The OPTN Contractor maintains a list of participating transplant programs.

4
5 If a participating transplant program chooses to split an accepted liver, the program will decide which
6 segment of the liver to transplant into the intended recipient. The transplant program must notify the host
7 OPO of the remaining segment prior to transplanting the remaining segment. The OPO must then offer
8 the remaining segment to the following potential transplant recipients, using the same match run used to
9 allocate the liver:

- 10 ▪ Lower-ranked status 1A and 1B potential transplant recipients registered at any transplant hospital
11 within 500 nautical miles of the donor hospital
12 ▪ Lower-ranked potential transplant recipients with a MELD or PELD of 33 or higher that are registered
13 at any transplant hospital within 500 nautical miles of the donor hospital

14
15 If the remaining segment is not accepted for any of the potential transplant recipients in the bulleted
16 classifications listed above, the OPO must notify the participating transplant program that accepted the
17 liver. The participating transplant program may then transplant the remaining segment into a different,
18 medically suitable, candidate registered at the same transplant hospital or an affiliated transplant program
19 with an active pediatric liver component. If the first segment is accepted for a pediatric potential transplant
20 recipient, the participating transplant program may transplant the remaining segment into a different,
21 medically suitable, candidate at the same transplant hospital or an affiliated transplant program. For
22 purposes of this variance, participating transplant programs may only have one affiliated transplant
23 program, and must identify the program they are affiliated with in their application for the variance.

24
25 If the participating transplant program declines the remaining segment, the OPO may offer the remaining
26 segment to any lower ranked potential transplant recipients off the same match run used to allocate the
27 liver to the recipient of the first segment.

28
29 *This variance shall expire three years after implementation.*

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