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Original Research

# Real-Time Assessment of Pulmonary Blood Flow in Pulmonary Vein Stenosis Using the Fluoroscopic Flow Calculator

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## ABSTRACT

**Background:** Restenosis in pediatric pulmonary vein stenosis (PVS) is common and requires careful monitoring. Lung perfusion scintigraphy (LPS) is often used but involves excess radiation, is resource-intensive, and can cause patient discomfort, with no real-time data available. This study evaluated the fluoroscopic flow calculator (FFC) as a real-time tool for estimating pulmonary blood flow (Qp) using angiograms during catheterization, with the potential to replace or complement LPS.

**Methods:** A retrospective cross-sectional study was conducted on patients with PVS who underwent cardiac catheterization between April 1, 2023, and March 31, 2024 at the Children's Hospital of Philadelphia. The study included patients who had a right ventricular angiogram and available LPS data. The FFC tool was used to analyze angiograms and estimate Qp distribution. Accuracy was assessed by comparing FFC predictions to LPS measurements using median absolute error and Bland-Altman analysis.

**Results:** The study included 21 procedures involving 18 patients, with a median age of 17 months. The FFC tool provided accurate predictions of Qp distribution, with a median absolute error of 3%. In 76% of cases, the predicted flow split was within 5% of the LPS measurement, and all cases were within 7%. Bland-Altman analysis revealed a minimal bias of +0.3%, with no systematic bias at the extremes of the flow-split distribution.

**Conclusions:** The FFC tool shows promise in estimating Qp distribution during cardiac catheterization in PVS patients. Further research is needed to refine the FFC method, particularly incorporating segmental lung information, and to evaluate its real-time use during catheterization.

## Introduction

Pediatric intraluminal pulmonary vein stenosis (PVS) is a chronic condition associated with significant morbidity and mortality.[1] Improved outcomes often necessitate serial transcatheter or surgical interventions; thus, continuous monitoring for recurrent PVS is essential for long-term management.[2] Nuclear lung perfusion scintigraphy (LPS) is commonly employed during surveillance, providing valuable insights into the distribution of pulmonary blood flow (Qp) between the right and left lungs or among different segments of the same lung. This imaging modality is particularly useful in detecting imbalances in blood flow caused by PVS and complements echocardiographic evaluations.[3,4]

The information provided by LPS is essential for longitudinal follow-up; however, it requires an additional test with additional exposure to ionizing radiation and can cause discomfort and anxiety due to vascular access and, in some cases, a lengthy imaging protocol.[5] For young patients, additional general anesthesia and mechanical ventilation may

*Abbreviations:* FFC, fluoroscopic flow calculator; LPA, left pulmonary artery; LPS, lung perfusion scintigraphy; PVR, pulmonary vascular resistance; PVS, pulmonary vein stenosis; Qp, pulmonary blood flow; RV, right ventricular.

*Keywords:* basic, translational, and clinical research; cardiac catheterization; imaging and diagnostic testing; lung perfusion scintigraphy; pulmonary vein stenosis; vascular disease.

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be required. Moreover, LPS data are not immediately available in the catheterization laboratory, where they might guide decisions about therapy. Until recently, however, the only alternative to an LPS was cardiac magnetic resonance imaging, which avoids radiation exposure but is more resource-intensive and time-consuming.

In previous work, we have described the development of a post-processing tool, the fluoroscopic flow calculator (FFC), which uses data from readily available angiograms to measure the relative distribution of Qp between the lungs.[6] The FFC tool is freely available and user-friendly, allowing an assistant to provide real-time input on whether additional interventions are needed. We sought to apply this tool to a cohort of patients undergoing transcatheter interventions for PVS, seeking for the first time to evaluate its real-world performance.

## Methods

### *Study population and design*

We conducted a retrospective cross-sectional study involving patients with PVS at the Children's Hospital of Philadelphia who underwent cardiac catheterization between April 1, 2023, and March 31, 2024. Inclusion criteria were availability of a postintervention right ventricular (RV) angiogram with anteroposterior angulation and a subjectively balanced view of both lung fields (a common practice for some operators, but not all), and a postprocedure LPS that was done within 60 days of catheterization.[6] If no interventions were performed, subjects with a preprocedural lung scan were also considered for inclusion. Patients who underwent any further interventions between the catheterization and the LPS were excluded. This study was reviewed by the Children's Hospital of Philadelphia's institutional review board, which approved the study and deemed it exempt from formal review and the requirement for informed consent. Deidentified data and statistical methods will be made available upon reasonable request.

### *Study measures*

For each procedure, data were collected from a manual review of angiograms, catheterization reports, and clinical records, and included the following: patient sex, date of birth, date of catheterization, indication for the procedure, number of pulmonary veins involved, presence of pre-existing stents, interventions performed (including whether a stent was placed), and whether the intervention was unilateral or bilateral (along with the number of veins treated). Additionally, preprocedural and postprocedural lung perfusion scintigraphy results were documented.

### *FFC*

As previously described, the FFC tool was created using Python and integrated as a new module within SlicerHeart, an open-source, cardiac-focused extension for the 3D Slicer medical image computing platform.[7,8] The FFC tool quantifies the total contrast present in each frame and within each lung field, focusing exclusively on the frames from the initiation of contrast injection and up to the moment just before the onset of the levophase. The total contrast added to each lung field in each frame is calculated by summing pixel intensities and subtracting baseline values. By aggregating these across all frames, the relative contribution of each lung to overall perfusion is determined. FFC was developed using a cohort of patients with conotruncal anomalies, in a retrospective study, and demonstrated strong correlation with LPS ($R^2$ = 0.83-0.87), without evidence of bias.[6]

### *Statistical analysis*

Characteristics of the study cohort were described using standard descriptive statistics. FFC measurements were compared to LPS and evaluated for accuracy and bias. Accuracy was measured using both the median absolute error and by calculating the percentage of predictions within 5% of the true flow split. Bias across the range of maldistribution of Qp was evaluated using the Bland-Altman analysis. All analyses were performed using Excel version 16.86 (Microsoft Corp) and R version 4.4.0 (R Foundation for Statistical Computing).

## Results

### *Study cohort*

A total of 82 interventional PVS procedures were performed during the study period. Of these, 21 procedures in 18 individuals met the inclusion criteria and were analyzed. The cohort had 56% male patients, with a median age of 17 months at the time of the procedure (range, 2 months to 12.2 years, Table 1). Multivessel PVS was present in 19 out of 21 cases (90%). In nearly all cases (20 out of 21, 95%), an intervention was performed on the pulmonary veins. The intervention targeted a single vein in 2 cases (10%), 2 veins in 11 cases (52%), and 3 or more veins in 7 cases (33%). Overall, bilateral interventions were performed in 12 out of 21 cases (57%). In 10 cases (48%), the patient had a pre-existing pulmonary vein stent, and in 3 cases (14%), a new stent was placed during the procedure.

### *Lung perfusion results*

Baseline perfusion data were available for 14 out of 21 procedures (67%). Among these, 13 procedures (93%) also had postprocedural perfusion data available. Additionally, there were 6 cases with post-procedural perfusion data but without baseline data, resulting in a total of 20 out of 21 cases (95%) with postprocedural perfusion data (Table 1). The postprocedural scan was performed 1 to 2 days after catheterization in 17 of the 20 cases, after 3 days in 1 case, and after 14 and 48 days in 2 other cases. In 1 case, no postprocedural LPS was obtained, but because no interventions were performed in that case, the final RV angiogram was compared to the preprocedural LPS. Among the 13 cases with both preprocedural and postprocedural perfusion data, 4 showed no improvement and 9 exhibited a median improvement of 4% (range, 2%-8%; Figure 1). Notably, in at least 1 case where an additional scan was performed a month later, with no interim interventions, the flow split improved from 27% to the left immediately postprocedure to 38% to the left, a month later.

### *Prediction model*

In all procedures, a nonselective RV angiogram was performed at the end of the procedure with a straight posteroanterior projection for flow calculations (Figure 2). Overall, the median difference (median absolute error) between the predicted and measured flow split was 3% (IQR, 2%-5%) (Figure 3). The predicted flow split was within 5% of the measured flow split in 16 out of 21 cases (76%). In 2 cases, the difference was 6%, and in 3 cases, it was 7%. In 1 case with a >5% discrepancy between fluoroscopy and lung perfusion scintigraphy—where FFC measured 33% to the left pulmonary artery (LPA) compared to 27% in the LPS—a repeat LPS performed a month later, with no further interventions in the interim, measured 38% flow to the LPA. In another subject, the LPS measured a flow of only 27% to the LPA versus 34% in FFC; however, chest x-ray during the LPS demonstrated atelectasis, low lung volumes, and interstitial edema on the left. The other 3

**Table 1.** Clinical characteristics and procedural details of the patient cohort

| IDX | Sex | Age (mo) | Multivessel disease? | Pre-existing stents? | New stent placed? | Bilateral intervention? | No. of veins intervened | LPS (pre) | FFC | LPS (post) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 6 | Yes | No | No | Yes | 2 | 58% | 50% | 54% |
| 2 | M | 107 | Yes | Yes | Yes | Yes | 2 | – | 63% | 66% |
| 3 | F | 19 | Yes | Yes | No | No | 2 | 22% | 26% | 25% |
| 4 | F | 101 | Yes | Yes | No | No | 1 | – | 31% | 28% |
| 5 | F | 11 | Yes | No | No | No | 2 | – | 33% | 40% |
| 6 | F | 80 | Yes | Yes | No | Yes | 2 | – | 19% | 13% |
| 7 | M | 146 | No | No | No | No | 0 | 45% | 46% | NA[a] |
| 8 | F | 7 | Yes | No | No | Yes | 2 | 42% | 45% | 40% |
| 9 | M | 7 | Yes | No | No | Yes | 2 | 30% | 31% | 36% |
| 10 | M | 7 | Yes | No | No | Yes | 3 | – | 33% | 27% |
| 11 | M | 68 | Yes | Yes | No | No | 2 | – | 72% | 72% |
| 12 | M | 15 | Yes | Yes | Yes | Yes | 3 | 39% | 40% | 37% |
| 13 | F | 27 | Yes | Yes | No | Yes | 3 | 24% | 34% | 27% |
| 14 | M | 19 | Yes | No | No | Yes | 3 | 27% | 30% | 32% |
| 15 | M | 9 | Yes | No | No | Yes | 4 | 33% | 34% | 41% |
| 16 | M | 7 | Yes | No | Yes | Yes | 3 | 38% | 39% | 37% |
| 17 | M | 71 | Yes | Yes | No | No | 2 | 37% | 44% | 39% |
| 18 | M | 2 | Yes | No | No | Yes | 3 | | 55% | 56% |
| 19 | F | 6 | No | No | No | No | 1 | 54% | 50% | 52% |
| 20 | F | 17 | Yes | Yes | No | No | 2 | 33% | 33% | 32% |
| 21 | F | 21 | Yes | Yes | No | No | 2 | 27% | 29% | 31% |

The table includes information on LPS values before and after the catheterization intervention, as well as the measured flow split based on the FFC at the end of the catheterization.
F, female; FFC, fluoroscopic flow calculator; IDX, case index; LPS, lung perfusion scintigraphy; LPS (pre), lung perfusion scintigraphy prior to catheterization; LPS (post), lung perfusion scintigraphy following catheterization; M, male.
[a] In this case, there was only preprocedural LPS data, yet no intervention was performed during catheterization.

cases did not have a clear explanation for the discrepancy between the measurement methods. Bland-Altman analysis demonstrated a bias of +0.3% (SE 4.2%) between the FFC-predicted split and LPS-measured flow split, with a maximum difference of 7% (Figure 4). The bias was not systematically worse at either extreme of the flow splits.

## Discussion

This retrospective cross-sectional study is the first to apply FFC for evaluating Qp distribution in PVS patients, demonstrating that FFC provides accurate predictions of flow split with minimal bias and no systematic error, even at extreme flow splits. This highlights the potential of FFC as a valuable clinical tool in this vulnerable population (Central Illustration).

Accurately measuring flow splits using angiograms during catheterization could significantly enhance the management of patients with PVS. By eliminating the need for postcatheterization LPS, hospitalization time can be shortened and radiation exposure minimized. Furthermore, baseline measurements at the start of the procedure could help better define the clinical status of patients referred for catheterization without up-to-date LPS data. This method also provides

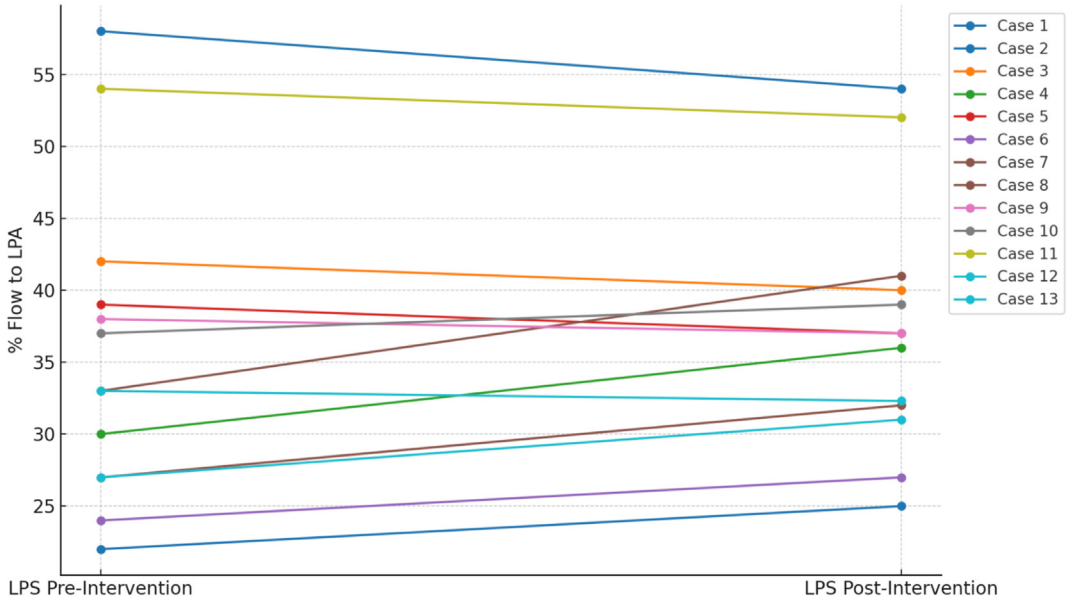



**Figure 1.**
**A slope chart depicting the change in lung perfusion scintigraphy (LPS) results before/after catheterization in the 13 cases with both pre–lung scans and post–lung scans.**
Case numbers are not the same as the numbers in Table 1 as these represent only cases with pre- and post-LPS data. LPA, left pulmonary artery.

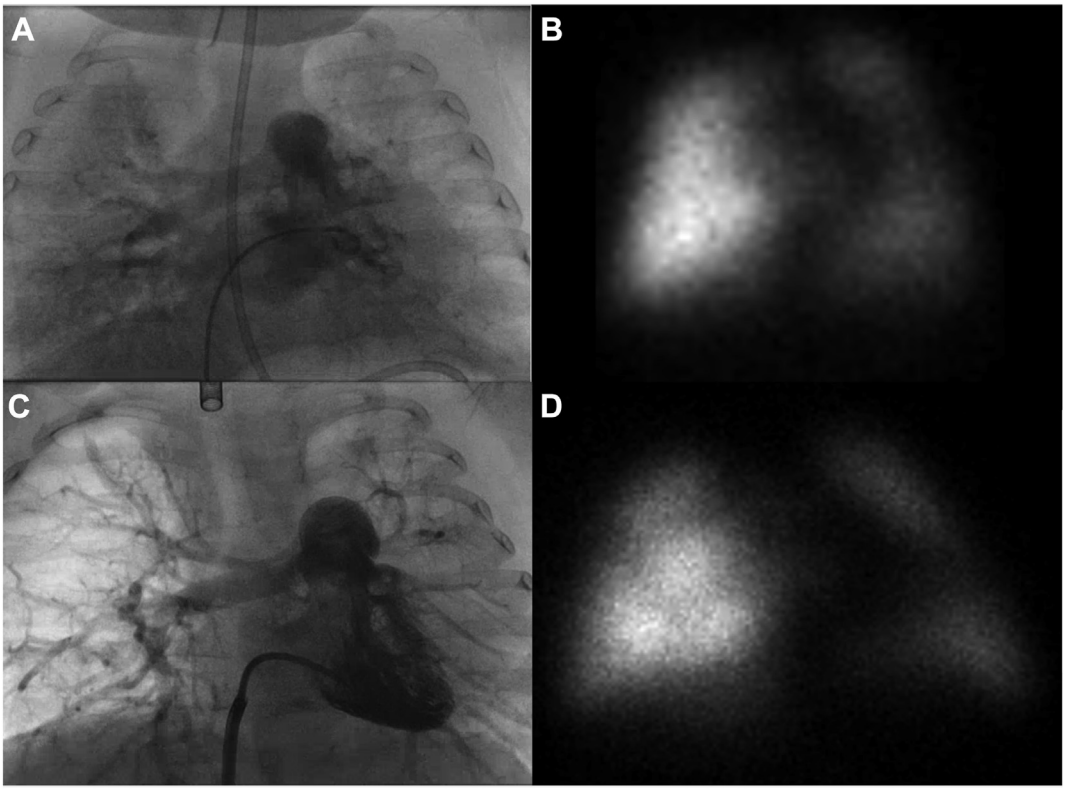



**Figure 2.**
**Example right ventricular (RV) angiograms and post-catheterization lung perfusion scintigraphy (LPS) studies for 2 patients: Subject #9 (A, B), with 31% flow to the left lung by RV-gram and 36% flow to the left by LPS, and subject #3 (C, D), with 26% flow to left by RV-gram and 25% flow to the left by LPS.**

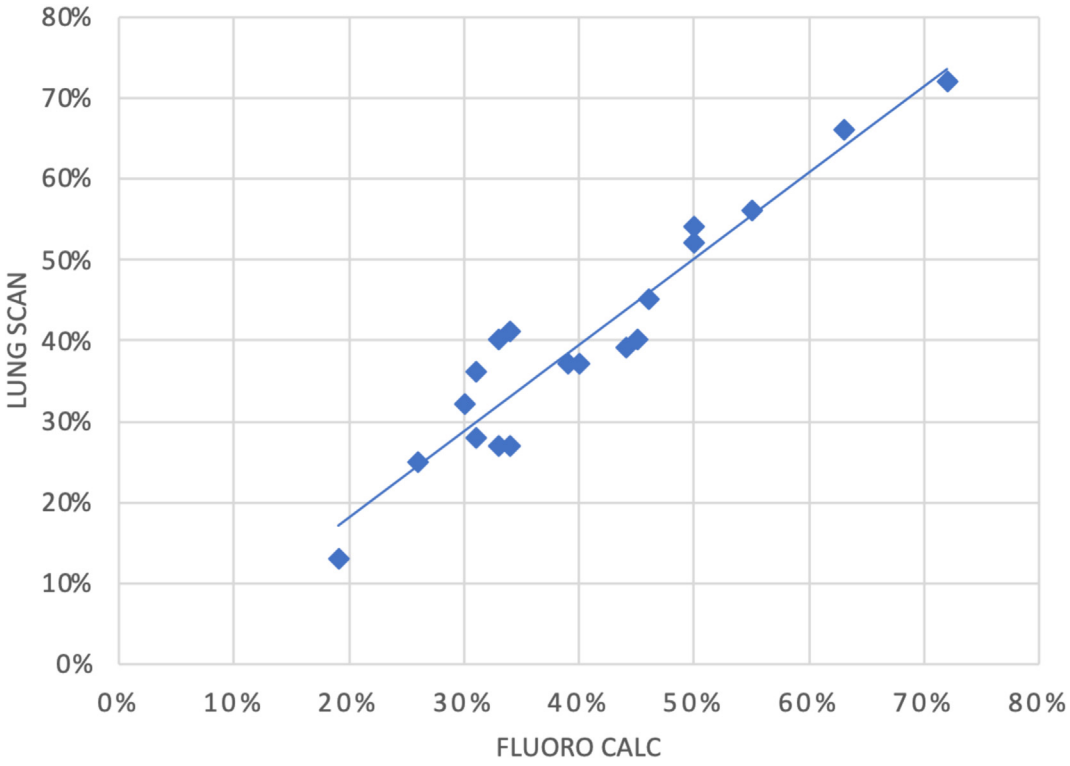



**Figure 3.**
**Percent of flow to the left pulmonary artery (LPA) as measured by the post-procedural lung scintigraphy (y-axis) vs the predicted split by fluoroscopy using fluoroscopic flow calculator (x-axis).**

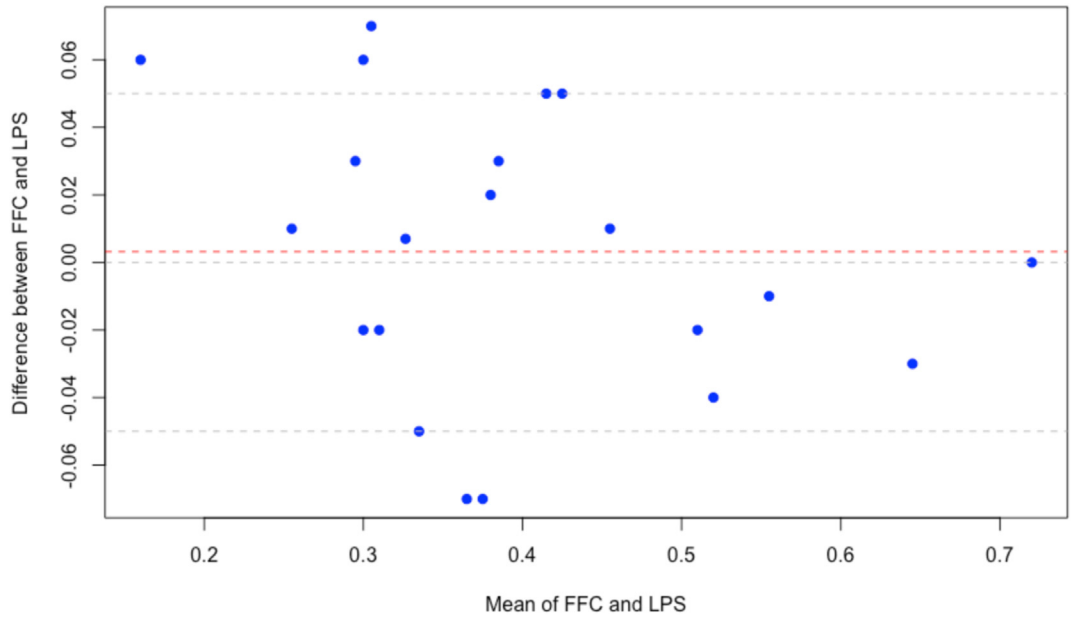
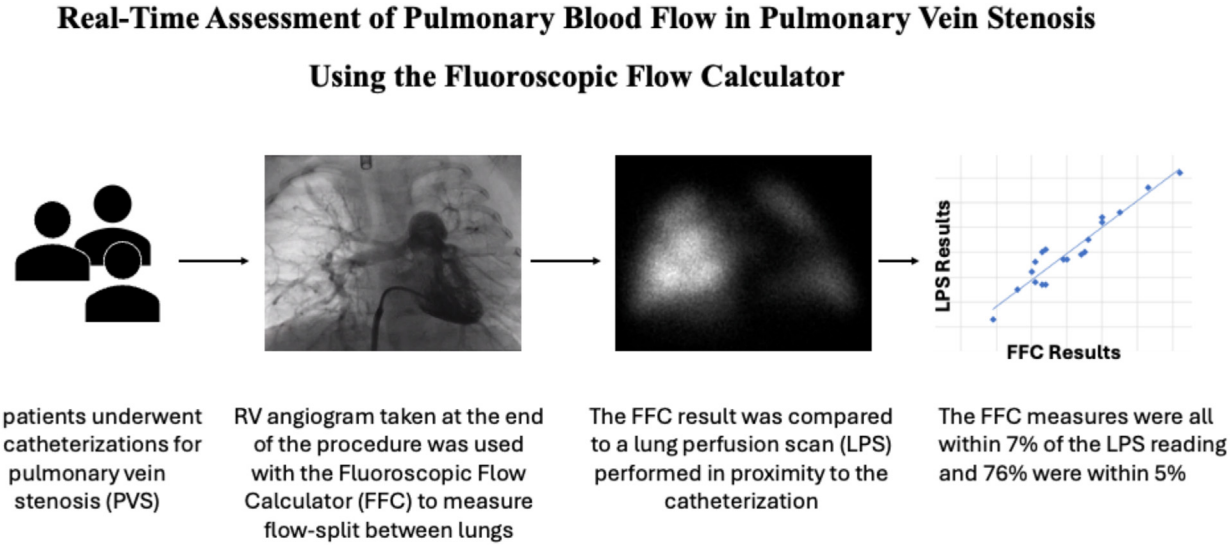



**Figure 4.**
**The Bland-Altman plot comparing the predicted values (fluoroscopic flow calculator [FFC]) and observed outcomes (lung perfusion scintigraphy [LPS]).** The plot shows the difference between FFC and LPS against the mean of the 2 measurements. The red dashed line represents the mean difference (+0.3%), and the gray dashed lines indicate 0%, +5%, and –5%. The analysis demonstrates that the bias is not systematically worse at either extreme of the distribution, with a maximum observed difference of 7%.

immediate feedback on the effectiveness of interventions, enabling more precise, goal-directed procedures. Flow-split measurement further allows for more accurate calculation of pulmonary vascular resistance (PVR) in patients with both PVS and elevated PVR. The current FFC method assesses the entire lung field, and further refining it to capture segmental information will be essential for achieving true clinical utility. While no technical limitations prevent this advancement, additional research is needed to develop and validate this capability.

The FFC method and the study we describe have several limitations worth noting. First, the study's retrospective design and small sample size require cautious interpretation of the findings. Nonetheless, these results build upon our previous work, providing additional support for our findings and for the accuracy of the FFC tool. Second, there are important differences between FFC and LPS measurements, such as the use of general anesthesia with endotracheal intubation during catheterization versus an awake, spontaneously breathing patient during LPS, the time gap between the 2 measurements, and the possible influence of diuretics and other medications that may have been administered during this interval. Third, single-ventricle PVS is a particularly high-risk population, which was not evaluated in this study. Possible unique challenges in these patients include nonpulsatile Qp and multiple sources of Qp, such as augmented Glenn shunts or systemic-to-pulmonary collaterals. Future studies are needed to better understand the utility of FFC in these complex scenarios. Fourth, the immediate postprocedural RV angiogram may not fully reflect the new physiologic baseline, as flow redistribution and PVR modulation may occur gradually over time following pulmonary vein interventions. Finally, while the use of an RV angiogram in these procedures is a




**Central Illustration.**
Eighteen patients underwent 21 catheterizations for pulmonary vein stenosis (PVS) where a right ventricular (RV) angiogram was taken at the end of the procedure. The RV angiogram was used with the fluoroscopic flow calculator (FFC) to measure the relative lung perfusion to each lung. Then, the FFC results were compared to a lung perfusion scintigraphy (LPS) performed in proximity to the catheterization. Overall, the FFC results were all within 7% of the LPS reading and 76% were within 5%.

common practice for some operators, it is not always performed during these catheterizations. Thus, the use of the FFC tool could require additional contrast and ionizing radiation exposure. However, it is important to note that LPS is also associated with significant radiation exposure (0.5-1.3 mSv).[9–12]

In summary, our findings highlight the potential of the FFC tool to accurately estimate Qp distribution in patients with PVS, potentially eliminating the need for postprocedural LPS. Furthermore, FFC offers real-time feedback to the interventionalist, enabling more precise, goal-directed procedures. Further research is needed to refine the FFC method, particularly to incorporate segmental lung information, and to evaluate its prospective applicability and real-time use during catheterization.

## Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethics statement and patient consent

This study was reviewed and approved by our institutional review board, which deemed it exempt from formal review and the requirement for informed consent. The research adhered to all relevant ethical guidelines.

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