Percutaneous Hepatic Perfusion for Liver Metastases: A Single Institutional Experience

Poster No.: C-3357  
Congress: ECR 2010  
Type: Educational Exhibit  
Topic: Interventional Radiology - Your latest results  
Keywords: interventional radiology, percutaneous hepatic perfusion, locoregional therapy  
Keywords: Interventional non-vascular, Interventional vascular  
DOI: 10.1594/ecr2010/C-3357

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

1) Understand the operational aspects of initiating a Percutaneous Hepatic Perfusion (PHP) program.

2) Lessons from a trial using melphalan to treat metastatic melanoma emphasizing initial patient selection, procedural considerations, post-operative management and patient follow-up.
Background

Ocular melanoma, much like its cutaneous cousin, has an excellent prognosis if detected and treated early in the disease process. However, once the disease has spread beyond the confines of the primary site, the associated disease related mortality escalates astronomically [1-3]. Ocular melanoma has a peculiar distribution of disease spread, with the initial and often sole site of extraocular disease confined to the liver [1-3]. For this reason, it was postulated by Alexander et al, that a locoregional therapy directed to the liver may provide significant survival advantage for patients with liver dominant disease. [4]

Initial work consisted of solitary liver treatments using open surgical hepatic isolation and high dose melphalan infusion. [4] While promising, it was clear from the early work that serial treatment strategy may provide a significant advantage over solitary treatments. Using the Delcath PHP™ System for hepatic isolation and hemofiltration, it is possible to functionally isolate the hepatic blood supply and blood return via a percutaneous approach. [5] This breakthrough technology recast hepatic isolation as a minimally invasive interventional technique completely amenable to repeat therapy. The Phase I and II US trial data was extremely promising and led to a large multi-center Phase III trial which is currently closed to new enrollment as it has maximally accrued. [5] Results from this trial will be submitted for FDA approval in the United States.

Our major goal in this report is to demystify this technique. First and foremost, this procedure requires a team approach. An experienced Interventional Radiologist, Anesthesiologist, Perfusionist and Surgical Oncologist are essential to the success of this program. While the hepatic isolation procedure is novel, most of the required catheter placements and pretreatment embolizations resemble other more common locoregional hepatic therapies, such as radioembolizations and chemoembolizations using drug-eluting beads. Manageable hemodynamic changes occur during the procedure, especially when the patient initially goes on by-pass, and then again when filtration is initiated. Management of these changes requires forethought and coordination between the specialties performing the procedure. Lastly, after discharge close follow-up with the patient is essential to minimize procedural side-effects and speed recovery.
Fig.: A Team Approach is Essential for Success

References: Radiology, University of Maryland Medical School - Baltimore/US

**Figure 1. A Team Approach is Essential for Success.** Our Institutional Approach is reflected in the accompanying illustration. The Surgical Oncology (HRA) was the senior most member of the team, with over 15 years of PHP experience, extending back to his NIH experience. Patient recruitment and selection was performed by him. As indicated by the thicker arrows, the PHP procedure was primarily the responsibility of the Perfusionist, Anesthesiologist, and Interventional Radiologist. Immediate post-operative recovery was managed by Anesthesia, but then care was transferred back to the Surgical Oncology team. Follow-up was primarily the responsibility of Surgical Oncology, but as
our experience grew, Interventional Radiology also began to assume a role in follow-up and patient management. Prior to initiating PHP treatments at our institution, a mentoring program with instructors from the NIH proctoring the involved physicians was instituted.

Fig.: Pretreatment Vascular Mapping and Collateral Embolization.

References: Radiology, University of Maryland Medical School - Baltimore/US

Figure 2. Pretreatment Vascular Mapping and Collateral Embolization.

The gastric and small bowel mucosa is exquisitely sensitive to melphalan. Therefore it is essential to eliminate collateral vessels originating from the hepatic arterial circulation that supply these structures. For patients enrolled in the trial, this is performed at the time of the initial PHP procedure. The gastroduodenal artery is often embolized. In one patient, a replaced left hepatic artery to the left gastric artery was present (Figure 2A, 2B). We elected to proceed with left hepatic artery embolization, to redirect left hepatic lobe perfusion to the intrahepatic collaterals originating from the right hepatic artery (Figure 2C, arrow marks the left hepatic artery). In a second patient, a prominent intrahepatic gastric collateral was present (Figure 2D, arrow) as well as a prominent right gastric artery (arrowheads). Embolization of the right gastric and intrahepatic collaterals was performed using coils (Figure 2E, arrow marks coils within the intrahepatic collateral).
Redirection of left hepatic flow simplified melphalan infusion because a single catheter infusion from the proper hepatic was then possible, as opposed to split therapy in the right and left hepatic artery territories.

**Fig.**: Percutaneous Hepatic Perfusion (PHP).

**References:** Delcath Systems, Inc. www.delcath.com

**Figure 3. Percutaneous Hepatic Perfusion (PHP).** The video clip dramatizes the PHP procedure. Enrolled patients underwent a series of PHP treatments with melphalan infused at 3 mg/kg. Sequential PHP treatments were performed at 5 week intervals until a treatment limiting side-effect forced trial curtailment.
Figure 4. Procedural Times Reflect the Procedural Learning Curve. Procedure times (in hours) were calculated from patient arrival to the Interventional Suite until transfer to the PACU or ICU (times were rounded to the closest quarter hour). The procedures are grouped by patient (the patients are numbered by their sequential entrance into the trial). The initial treatment is shown in red, while subsequent treatments are in shades of blue. The data demonstrate two clear trends. First, there is a procedural learning curve as noted by the overall extended procedure times for the first patient compared with subsequent patients. Also evident is the increased time for each initial case. This is secondary to the required time for anatomic mapping and collateral embolization.
Fig.: Treatment Associated Side-effects Were Secondary to Systemic Exposure to Melphalan

**References:** Radiology, University of Maryland Medical School - Baltimore/US

Figure 5. Treatment Associated Side-effects Were Secondary to Systemic Exposure to Melphalan. The table breaks down the observed side-effects by patient. The treatment number signifies the treatment after which the side-effect was observed. In our experience, the major side-effects are related to acute bone marrow suppression. One patient experienced severe gastritis with marked weight-loss.
Images for this section:

**Fig. 0:** A Team Approach is Essential for Success

© Radiology, University of Maryland Medical School - Baltimore/US
Fig. 0: Pretreatment Vascular Mapping and Collateral Embolization.

© Radiology, University of Maryland Medical School - Baltimore/US
Fig. 1: Percutaneous Hepatic Perfusion (PHP).

© Delcath Systems, Inc. www.delcath.com
**Fig. 0:** Procedural Times Reflect the Procedural Learning Curve.

© Radiology, University of Maryland Medical School - Baltimore/US
**Fig. 0:** Treatment Associated Side-effects Were Secondary to Systemic Exposure to Melphalan

© Radiology, University of Maryland Medical School - Baltimore/US
Conclusion

Percutaneous Hepatic Perfusion using the Delcath PHP™ System is an exciting new entrant into the locoregional therapeutic arsenal in the fight against hepatic metastases. [5] The technique purports to allow delivery of high-dose chemotherapeutic agents into the hepatic circulation while simultaneously minimizing the systemic exposure to these agents. Early Phase trials using melphalan as the infused agent have shown this technique to be effective against a wide range of cancer types, including neuroendocrine, hepatocellular, colorectal and melanoma. [6] The Institutional experience that we report here was as part of a Multi-center Phase III trial for the treatment of metastatic melanoma.

Our approach began with a carefully selected team, which included an experienced Surgical Oncologist, Anesthesiologist, Perfusionist, and an Interventional Radiologist. Each of our team members received mentoring from physicians at the NIH who were currently performing the PHP procedure. This mentoring reduced the learning curve for overcoming procedural pitfalls as we were able to more adequately predict and manage these procedural challenges. Similarly, choosing an Interventional Radiologist with prior experience performing drug-eluting bead chemoembolization and radioembolization reduced the learning curve for the PHP procedures because many of the pre-treatment goals are shared between these techniques. Specially, detecting and embolizing intrahepatic and peri-hepatic collaterals supplying the stomach, small bowel and pancreas. In our experience, after only a few PHP procedures, our team was able to significantly reduce the procedural times, both for initial PHP procedures and sequential procedures. Overall, the procedure was well tolerated with the most common side-effects being thrombocytopenia and anemia. These were successfully managed with Neupogen and occasional transfusions.

With diligent institutional preparation and team member training, this procedure can be successfully incorporated into the mainstream treatment strategy for hepatic metastases. The early published results for this therapy are encouraging, and we are eagerly awaiting the results from the current Phase III trial. However, if our experience is at all indicative, broad acceptance of this procedure is forthcoming both in Europe and in the United States.
Corresponding author: Fred M. Moeslein, MD, PhD, Assistant Professor of Radiology at the University of Maryland Medical School, Baltimore, MD 21201. Email: fmoeslein@umm.edu
References


