NO LOSS OF HUMAN (MANTLE-) ISLETS BY OPTIPREP-UWS PURIFICATION FOLLOWING ISOLATION IN UWS

Michel P.M. van der Burg, Jan Ringers, André Baranski,
Eelco Bouwman, and Onno T. Terpstra

Department of Surgery
Leiden University Medical Center
Netherlands

BURG@LUMC.NL

Human islet purification is hampered by many donor and isolation factors ....

that may lead to :

…e.g. deterioration of the density difference between islets and acini ,

…or the isolation of islets still covered with a mantle of acinar cells — “mantle islets” —

which generally results in a poor purity and islet loss after density separation .

We recently reported > 80% purity & recovery after purification in our gradient of OptiPrep*- UWS

In this first series of 5 experiments the human islets were

- isolated by the automated method,
- collected in cold RPMI, and
- incubated 1 hour in UWS before the gradient separation

The digest in this series contained however ~ no mantle-islets.

Van der Burg MPM, Ranuncoli A, Molano R, Kirlew T, Ringers J, Bouwman E, Ricordi C. Efficacy of the novel iodixanol-UWS density gradient for human islet purification (Abstract). Acta Diabetol 1998; 35: 247

*OptiPrep is a 60% iodixanol solution produced by Nycomed (Oslo, Norway)

We now report the efficacy of the OptiPrep- UWS gradient in 6 consecutive experiments performed with the simple manual digestion method, that ...

…facilitated testing, whether using the UWS during all cold steps better preserves the tissue, and,

…further — because of the high proportion of mantle-islets in this study — allowed us to test whether the gradient may also save these islets from pelleting with the acinar tissue.

PROCEDURE

Pancreases

- procured from multiorgan (13–58 y) donors, and
- cold preserved with UWS for 3–11 h, were
- digested at 37°C by static incubation 21–32 min with Liberase-HI (1.4 mg/ml) in Hanks

The digest was dispersed in cold UWS (ViaSpan) by shaking and sieving (500 μm), and a sample was taken for assessment and -->

Purification in “test-gradients” in 15-ml conicals

Bulk purification in gradients (bottom - barrier - UWS) with

- bottoms varying from 1100–1080 g/L
- barriers varying from 1090–1072 g/L

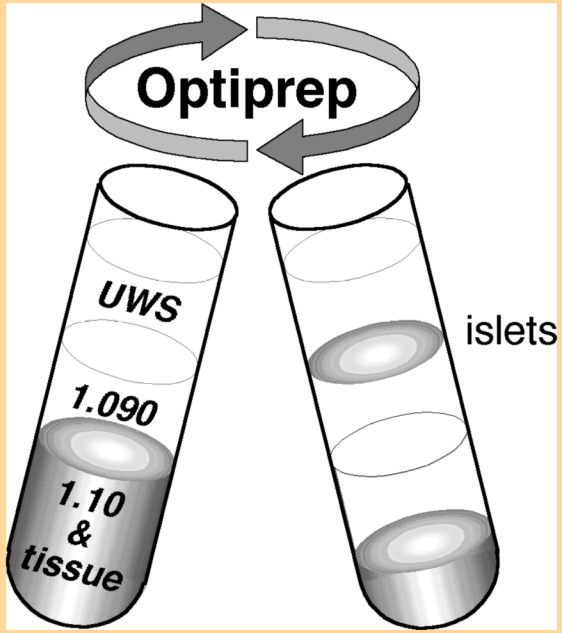
RECIPE FOR THE OPTIPREP—UWS GRADIENT

OptiPrep is a 60% iodixanol in H_2O solution

Working OptiPrep solution (WOP)
is prepared by mixing equal volumes of
- OptiPrep, and
- double-strength UWS (UWS 2x)

E.g. an 1100 bottom is made by mixing
- 200 ml digest (in UWS) and
- 100 ml WOP

E.g. an 1090 barrier layer is prepared by mixing
- 200 ml UWS and
- 76 ml WOP



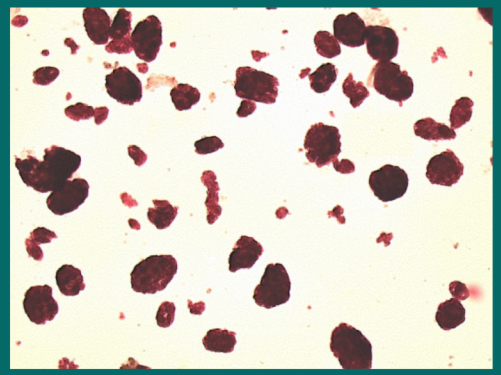
After 5 min centrifugation at 4°C and 500 *g*, collect islets from the 1st (-2nd) interface

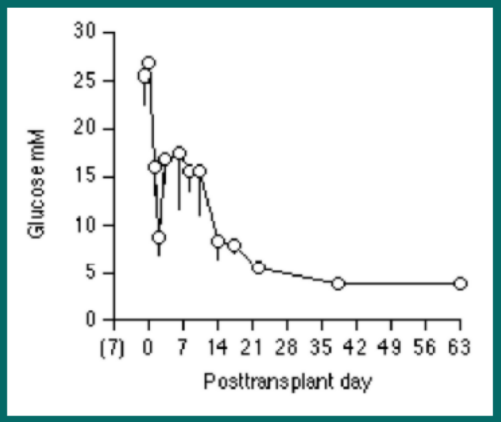
RESULTS...

After density separation islets including mantle-islets were recovered at a density < 1075, 1080, 1090, 1086, 1100, 1086 resp. during consecutive experiments.
Mean 'barrier' density: 1086 g/L

On average:

	DIGEST	GRADIENT
IEQs/g (% recovery)	1797 ± 410	1702 ± 334 (104%)
% MANTLE-ISLETS	38 (10–60)	1st L: 14% / 2nd L 89%
DIAMETER (*µm*)	163 ± 7	167 ± 11
% PURITY (+ mantle)		85 ± 7 (74%)





Glycemia 2 mo after SRC Tx in nude mice

Powerful Tool for Human Islet Purification

Thus, the consistent high efficacy of the simple OptiPrep-UWS gradient: no loss of islets, mantle islets, and a high purity

& the favorable characteristics such as

- the mild hyperosmotic conditions (~380 mOsm)
- a low endotoxin content
- the clinical safety-tested components

suggest the gradient to be a powerful new tool for human islet purification.

Nycomed plans to produce a similar working Optiprep-UWS soon.

Notes

Notes added in this online reprint July 5, 2026

- Oral presentation at the 19th Workshop of the Study Group on Artificial Insulin Delivery Systems, Pancreas and Islet Transplantation (AIDSPIT) of the European Association for the Study of Diabetes (EASD) in Igls, Austria, January 23–25, 2000
- Abstract : 19th Workshop of the Study Group on Artificial Insulin Delivery Systems, Pancreas and Islet Transplantation (AIDSPIT) of the European Association for the Study of Diabetes (EASD) . *Acta Diabetol* **36**, 205–231 (1999). https://doi.org/10.1007/s005920050168
- Optiprep and UW2x were replaced by the approved medicinal products Visipaque and Viaspan in the 2001 Standard Operating Procedures for use in the GMP cleanroom facility of our Clinical Islet Laboratory in the LUMC (Leiden).
- Citation info : No Loss of Human Islets • AIDSPIT 2000 • 1MEMO_20260705_4 • Michel van der Burg • Miracles•Media