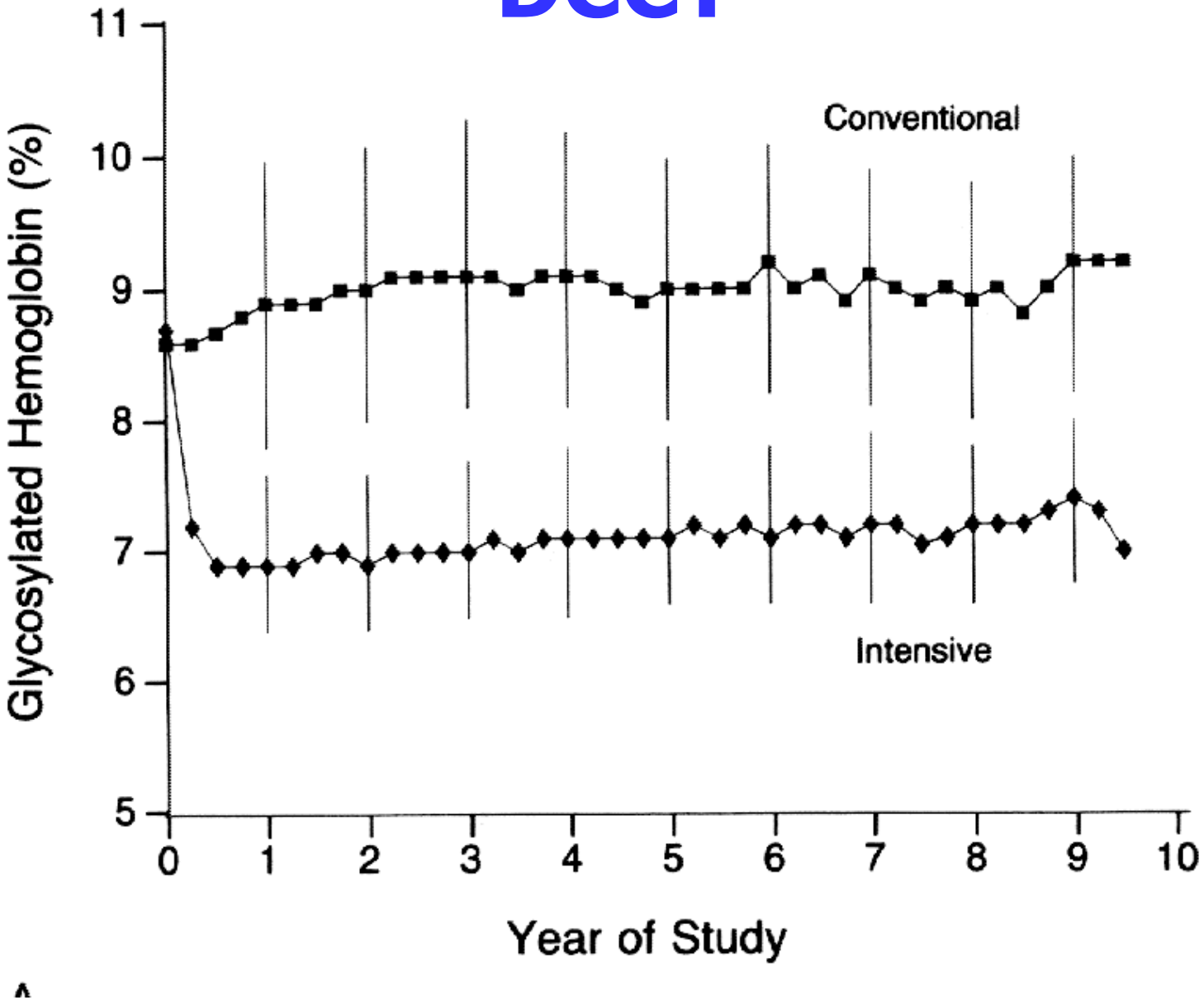
Improving Control through Better Injections

r. Ken Strauss

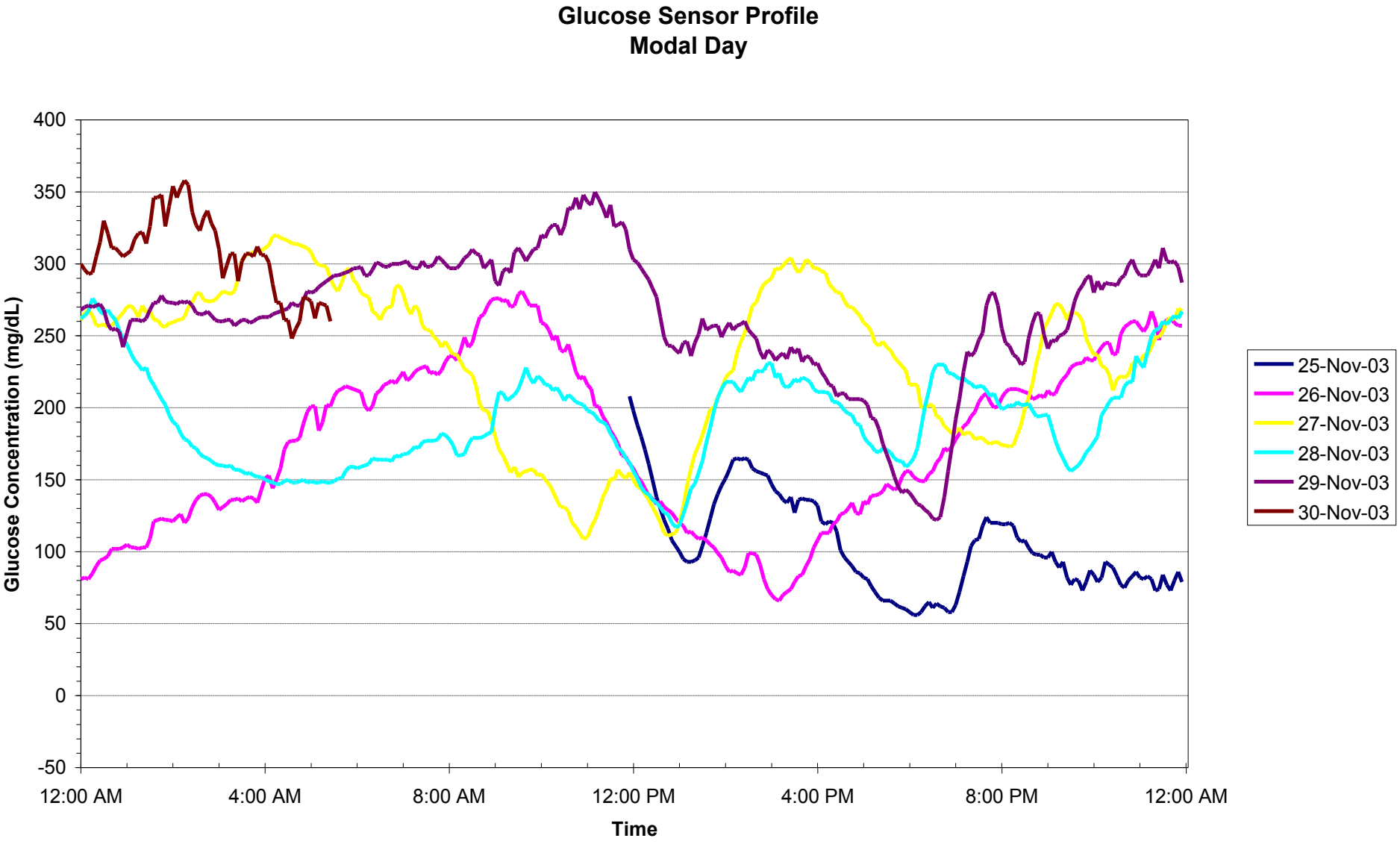
Baveno, Oct. 25, 2014

DCCT

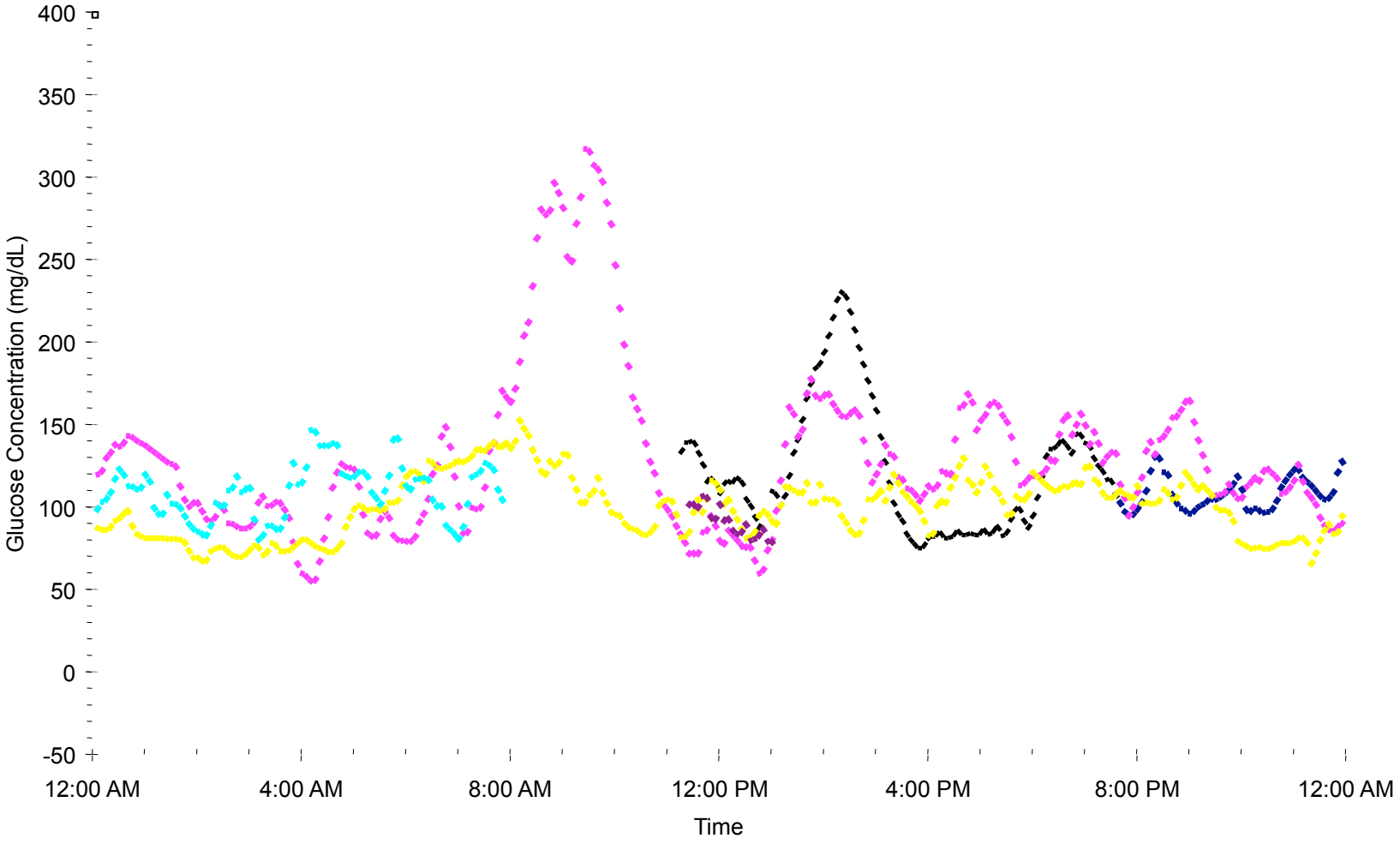


NEJM, 1993

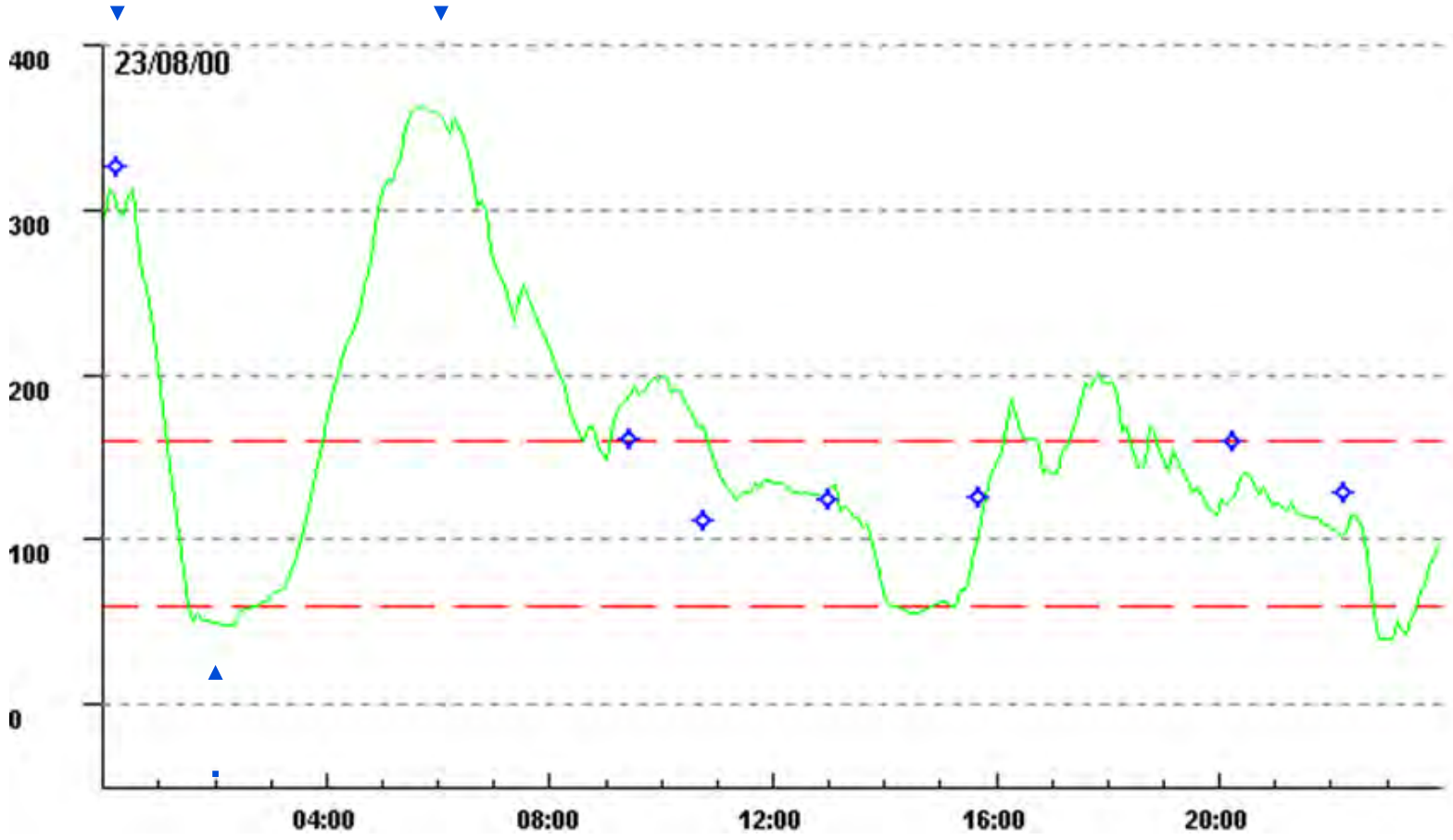
Glucose Variability



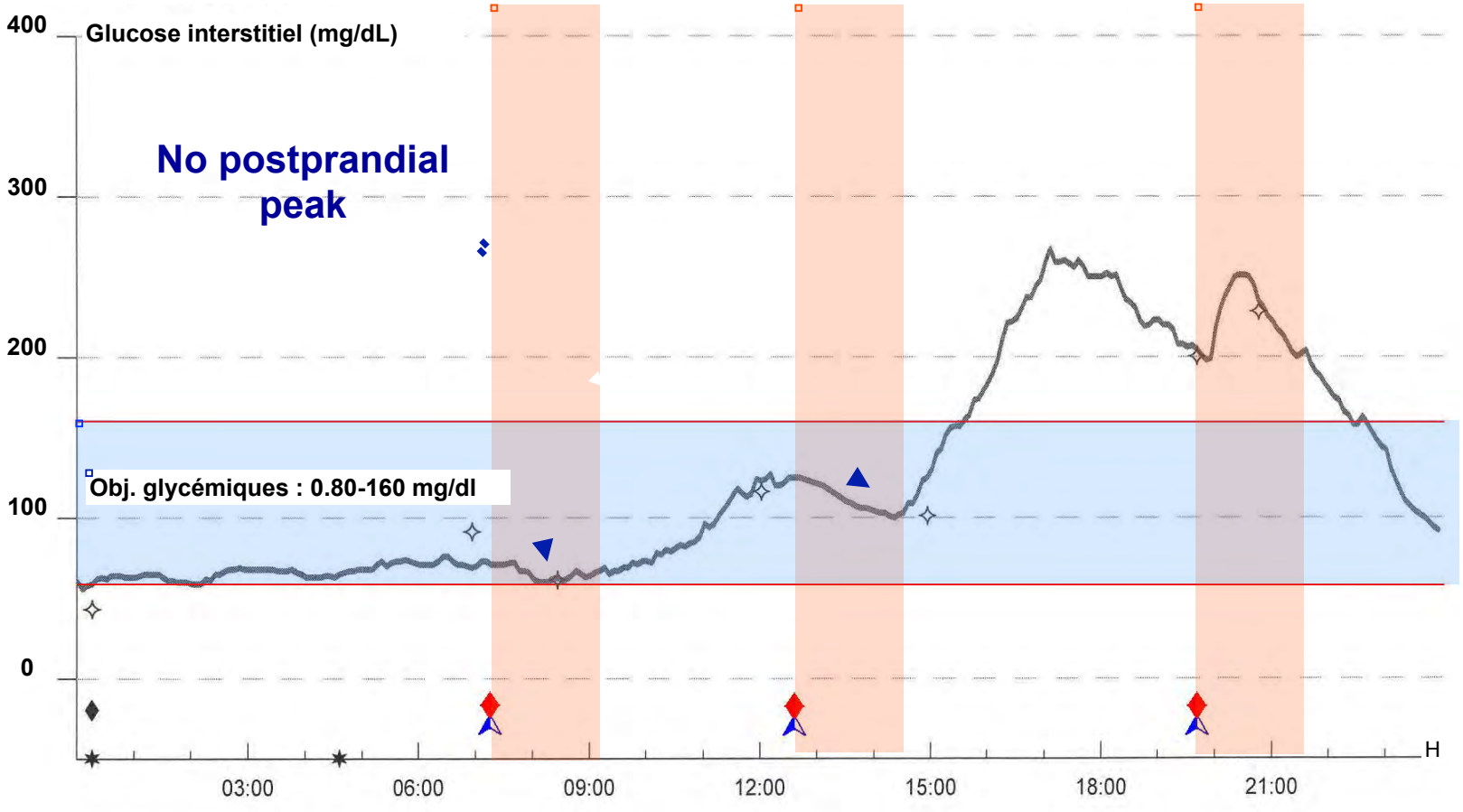
Omission of a bolus



Over-Correction



Gastroparesis



Meal

Bolus of insulin

Other Causes of Variability

Inappropriate dosing of insulin

Inappropriate injection of insulin

Dietary or exercise indiscretions

Other stressors

Lipohypertrophy

Seven landmark studies

1. Frequency
2. Causes
3. Histopathology
4. Absorption
5. Glucose control
6. Insulin reductions
7. Cost savings

LH is common

15.9% (Kashi et al 2008)

27.1% (Raile et al. 2001)

34.5% (Partanen, Rissanen 2000)

48.0% (Kordonuri et al 2002)

57.0% (Teft 2002)

Have you ever noticed swelling of fatty tissue or small bumps at your injection sites?

48%

said yes*

*2009 ITQ Survey

44,6	USA
44,6	RUSSIA
45,6	NETHERLANDS
54,2	BELGIUM
50,4	FRANCE
51,7	SPAIN
44,6	ITALIA
73,3	SWITZERLAND
54,2	UK & IRELAND
56,6	DENMARK
60,0	SWEDEN
52,2	GERMANY
31,1	CHINA
33,1	TURKEY
30,0	PORTUGAL
88,0	FINLAND

De Coninck C, et al. Results and analysis of the 2008-2009 Insulin Injection Technique Questionnaire survey. J Diabetes. 2010 Sep;2(3):168-79.

What is your experience?

Seven landmark studies

1. Frequency
2. Causes
3. Histopathology
4. Absorption
5. Glucose control
6. Insulin reductions
7. Cost savings

ELSEVIER

Diabetes Research and Clinical Practice 77 (2007) 231–236

www.elsevier.com/locate/diabres

Incidence of lipohypertrophy in diabetic patients and a study of influencing factors

Bahar Vardar [a], Sevgi Kızılcı [b,*]

Results:

Frequency lipohypertrophy **: 48.8%**

Three independent risk factors :

1. **Using insulin for long time (p=0.001),**
2. **Giving injection in same place (p=0.004),**
3. **Reusing the same needle (p=0.004).**

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Seven landmark studies

1. Frequency
2. Causes
3. Histopathology
4. Absorption
5. Glucose control
6. Insulin reductions
7. Cost savings

Endocrine Journal 2005, **52** (5), 623–628

Insulin-induced Lipohypertrophy: Report of a Case with Histopathology

JUNJI FUJIKURA, MUNEYA FUJIMOTO, SHINTARO YASUE, MICHIO NOGUCHI, HIROAKI MASUZAKI, KIMINORI HOSODA, TAKAO TACHIBANA*, HAJIME SUGIHARA** AND KAZUWA NAKAO

Department of Medicine and Clinical Science, Division of Endocrinology and Metabolism, Kyoto University Graduate School of Medicine, Kyoto 606-8507, Japan

**Department of Dermatology, Tenri Yorozu Hospital, Nara 632-8552, Japan*

***Department of Pathology, International University of Health and Welfare, Okawa 831-0004, Japan*

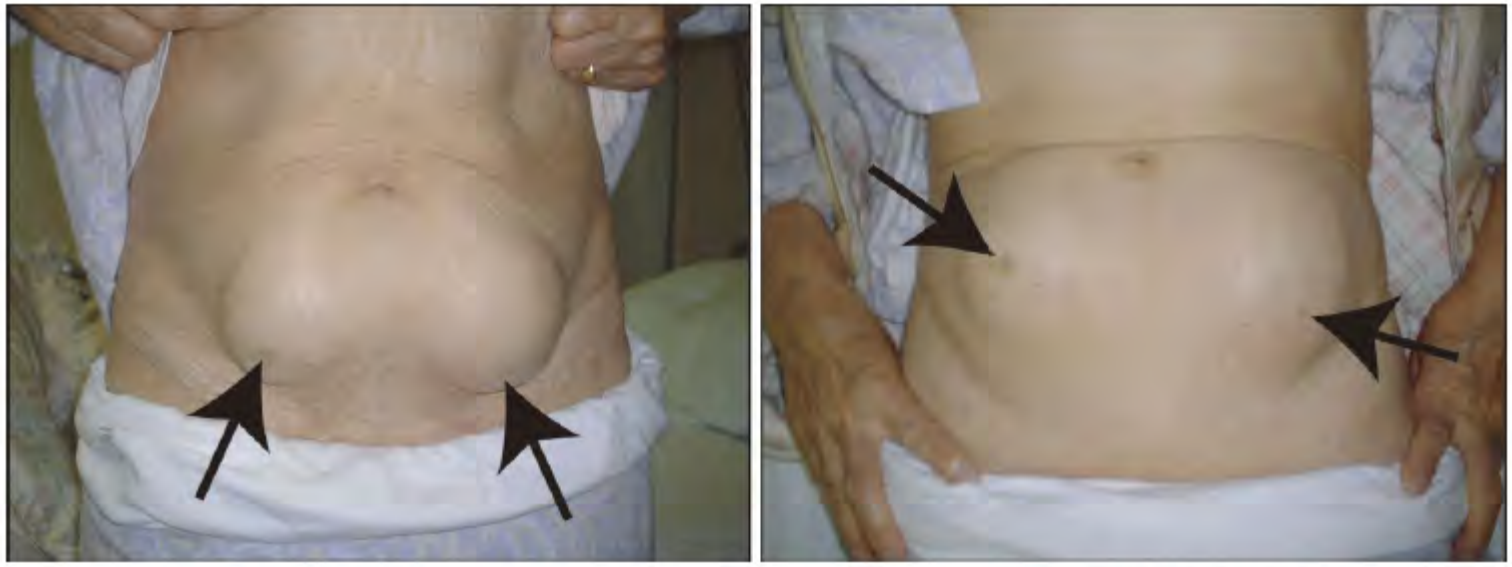


Fig. 1. Large movable abdominal masses. Pictures were taken in two body positions, standing (left) and spine (right). There are scars at the sites of insulin injections (arrows).

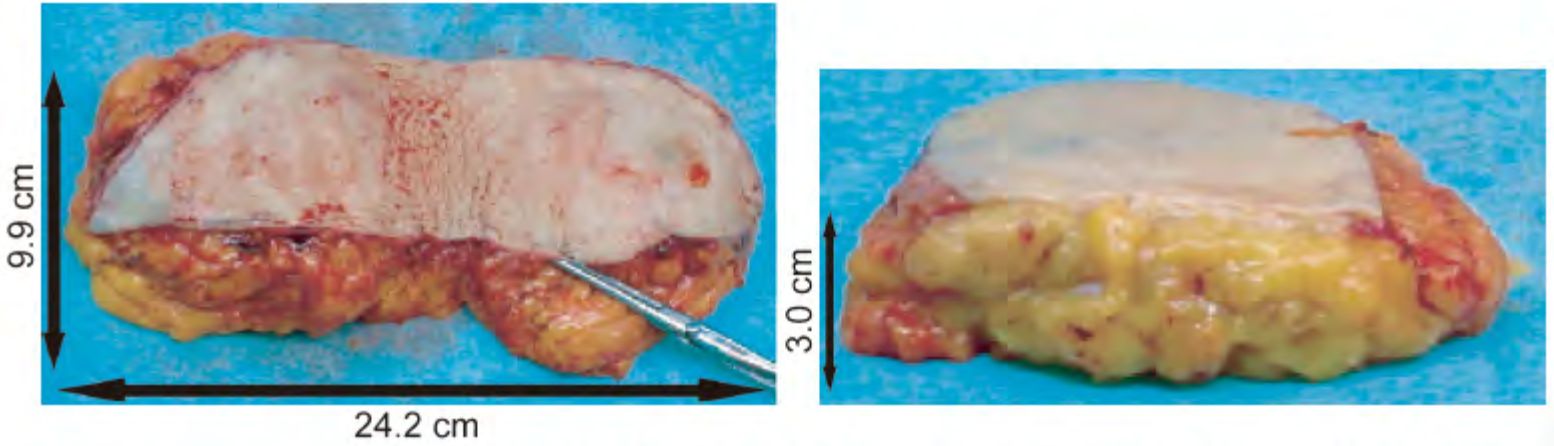


Fig. 2. Surgically resected specimen. Outside view (left) of the whole specimen and a cross-sectional view (right) of the specimen. The two masses were composed of yellowish fatty tissues and were not encapsulated by fibrous tissues.

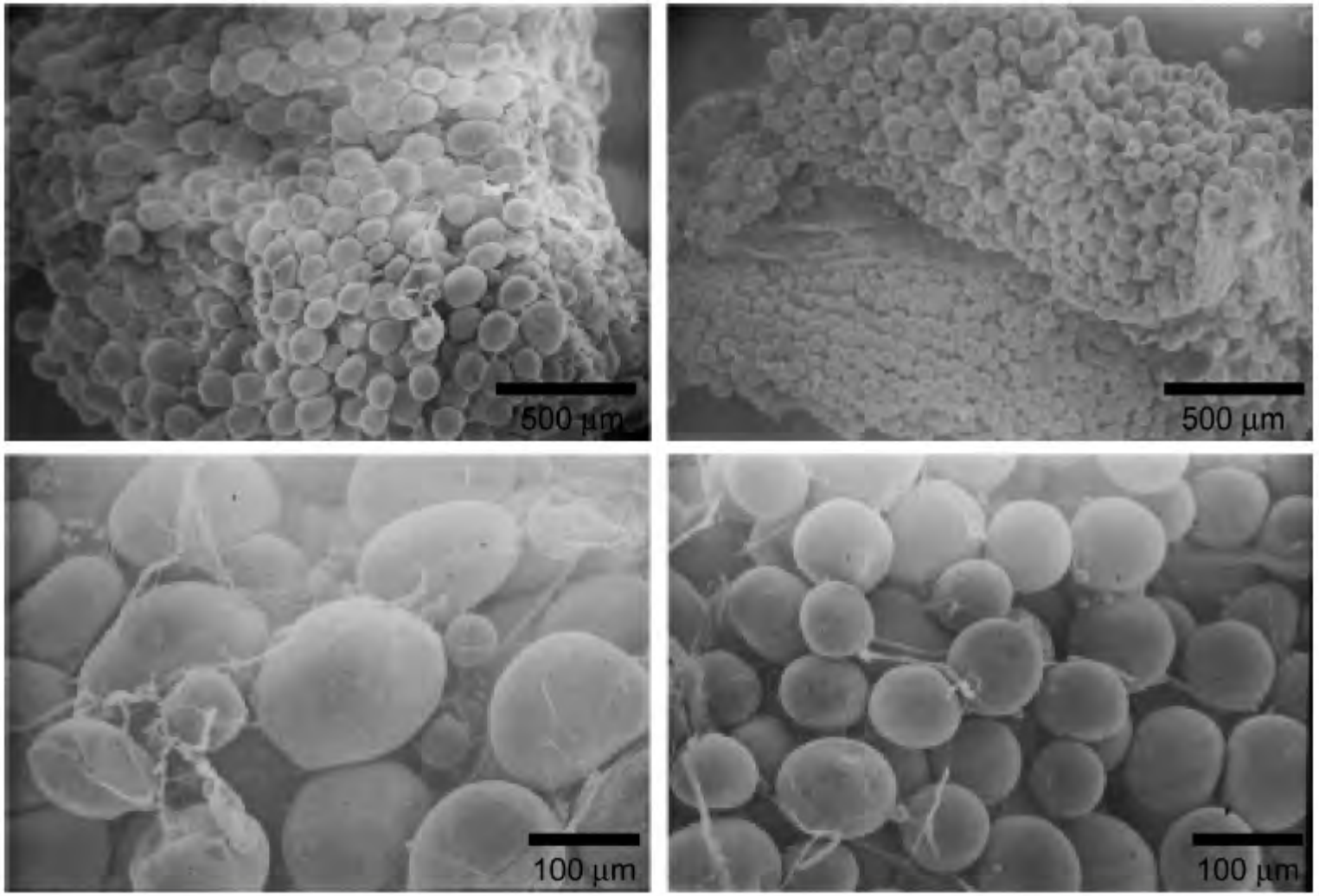


Fig. 4. Hypertrophic adipocytes. Scanning electron microscopy of the insulin-induced lipohypertrophy (left) and adjacent normal subcutaneous adipose tissue (right) at magnifications of ×50 (upper) and ×100 (lower).

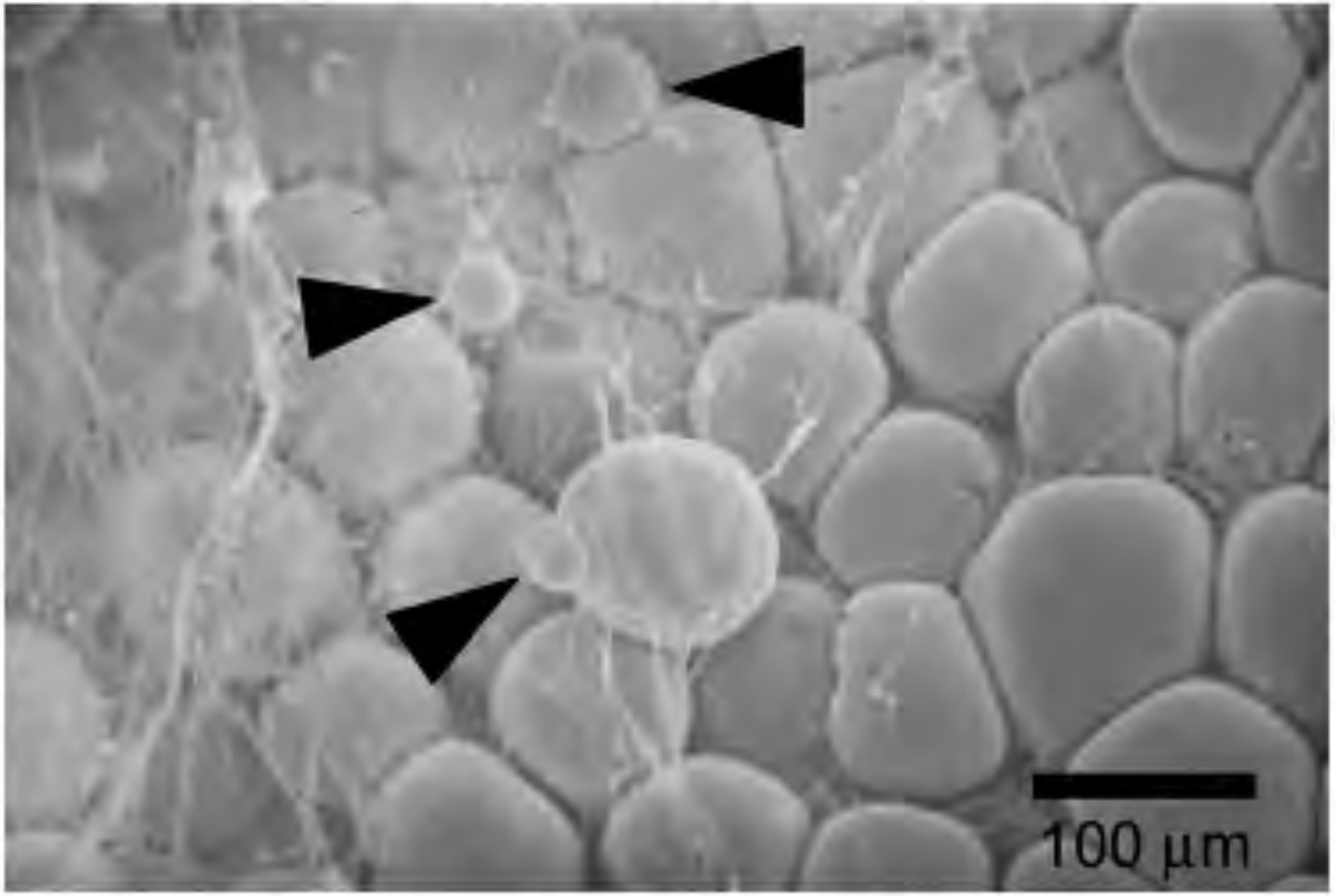
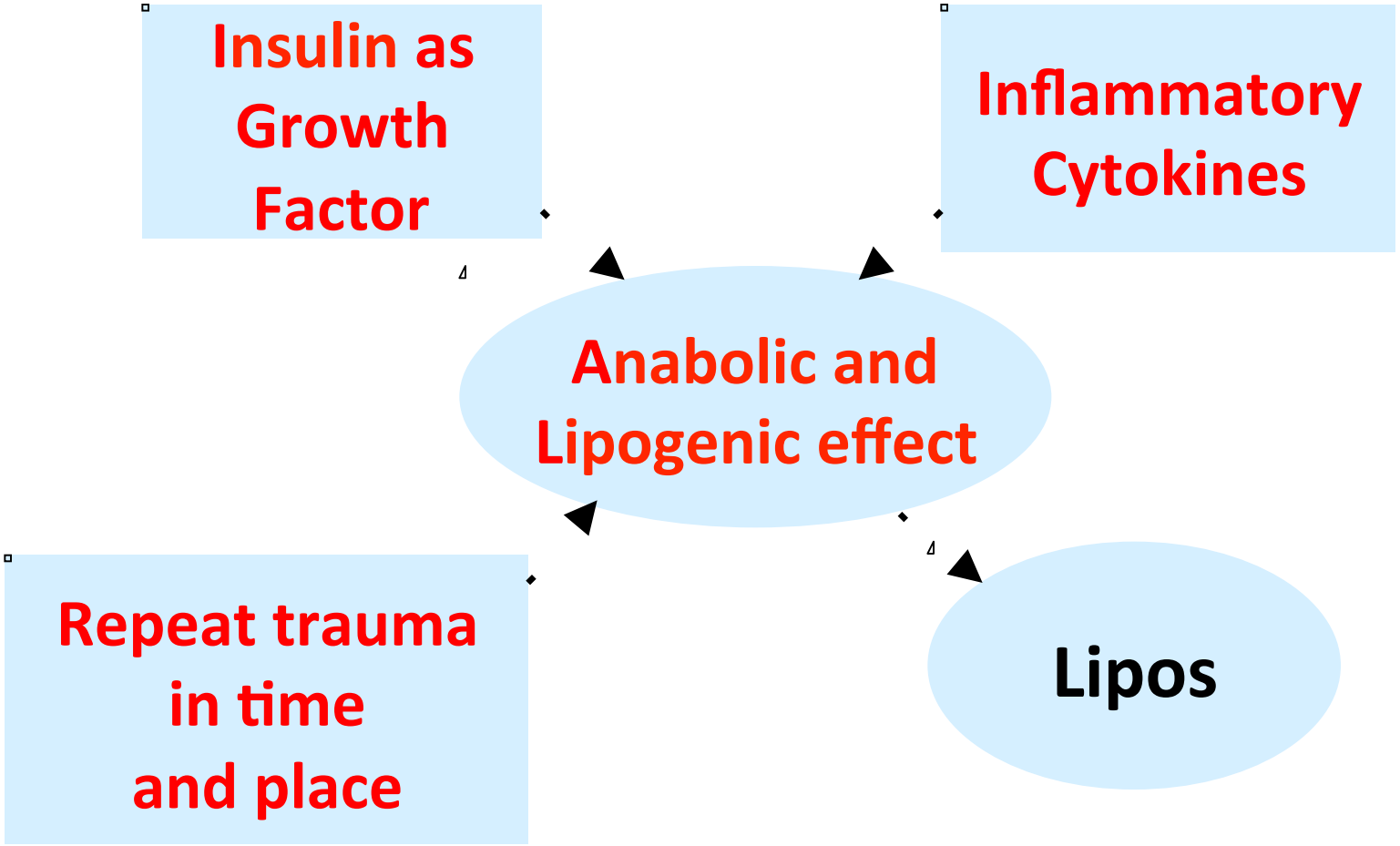


Fig. 6. Heterogeneous size of adipocytes in the insulin-induced lipohypertrophy. Arrowheads in the SEM (magnification: ×200) image indicate small adipocytes.

Possible Causation Model



How is insulin absorbed in lipohypertrophy?

Seven landmark studies

1. Frequency
2. Causes
3. Histopathology
4. Absorption
5. Glucose control
6. Insulin reductions
7. Cost savings

Clinical Care/Education/Nutrition

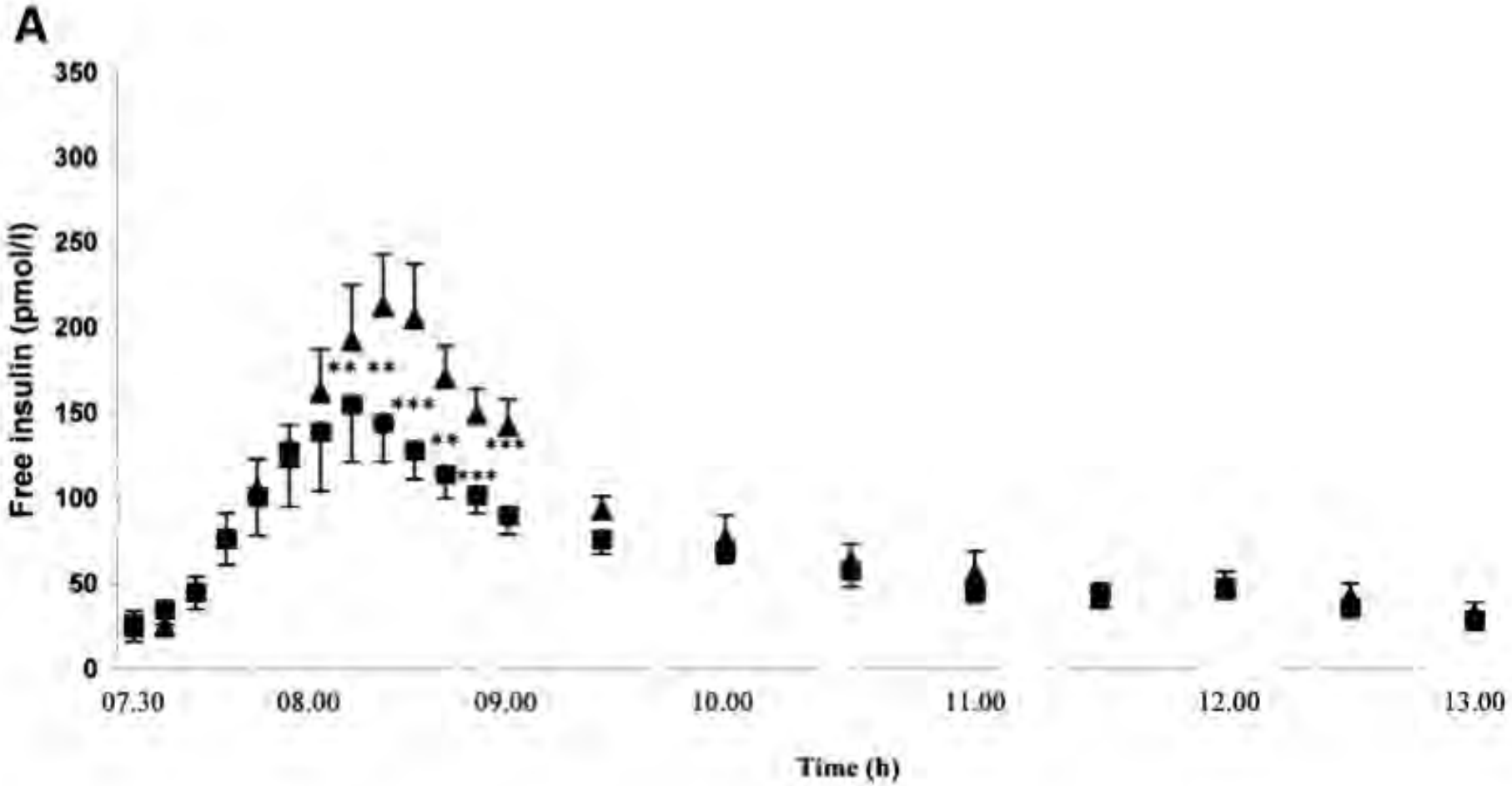
BRIEF REPORT

Impaired Absorption of Insulin Aspart From Lipohypertrophic Injection Sites

UNN-BRITT JOHANSSON, RN, PHD[1,2]
SUSANNE AMSBERG, RN[2]
LENA HANNERZ, RN[2]
REGINA WREDLING, RN, PHD[2,3]
ULF ADAMSON, MD, PHD[2]
HANS J. ARNQVIST, MD, PHD[4]
PER-ERIC LINS, MD, PHD[2]

performed two absorption tests in random order separated by a minimum of 7 days. Patients arrived at the clinical research center at 7:30 A.M. after an overnight fast of no less than 7 h. An indwell-

Diabetes Care 2005; 28:2025-2027


A
350
300
250
200
150
100
50
0
Free insulin (pmol/l)
07.30
08.00
09.00
10.00
11.00
12.00
13.00
Time (h)

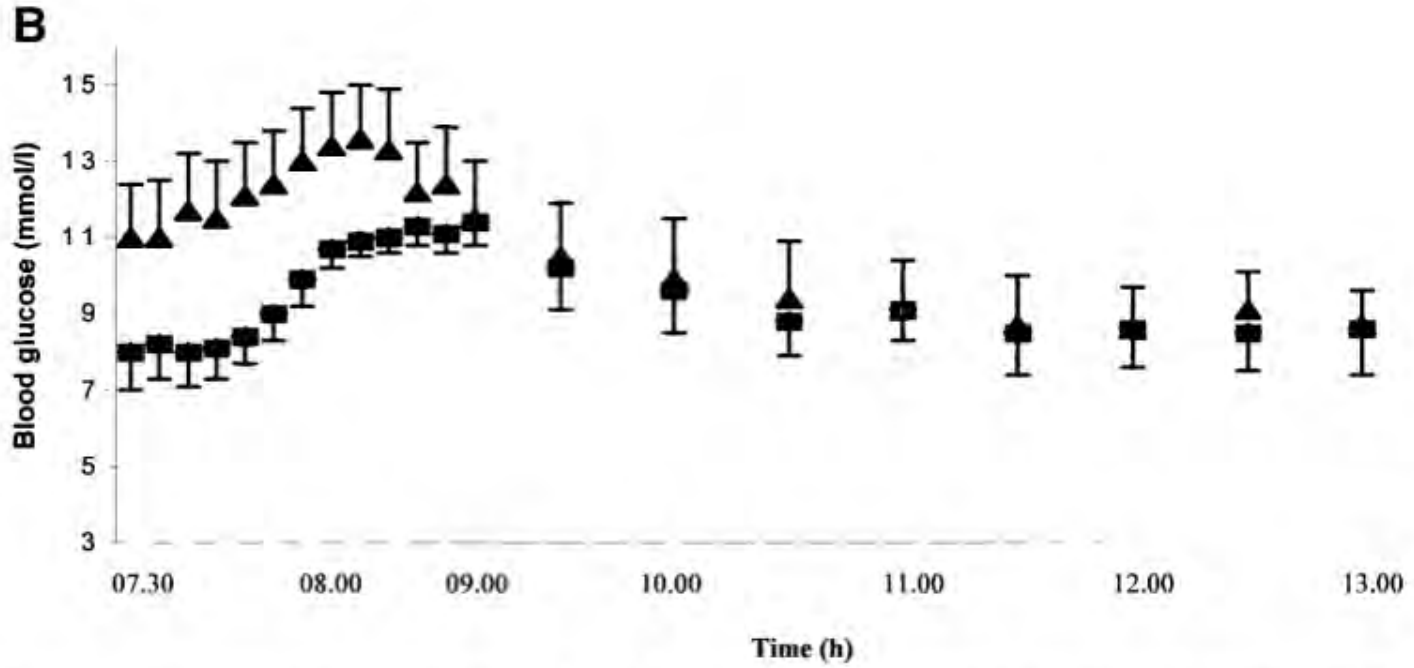


Figure 1—*Plasma concentrations of free insulin (A) and blood glucose (B) in nine type 1 diabetic patients after a 10-unit subcutaneous injection of insulin aspart in normal tissue (▲) versus lipohypertrophic tissue (■) at 7:30 A.M., immediately before breakfast. Values are means ± SE.* *P < 0.05, **P < 0.01, ***P < 0.001.

Journal of Diabetes Science and Technology
Volume 4, Issue 3, May 2010

COMMENTARY

Insulin Absorption from Lipodystrophic Areas: A (Neglected) Source of Trouble for Insulin Therapy?

Lutz Heinemann, Ph.D.

Medtronic ®

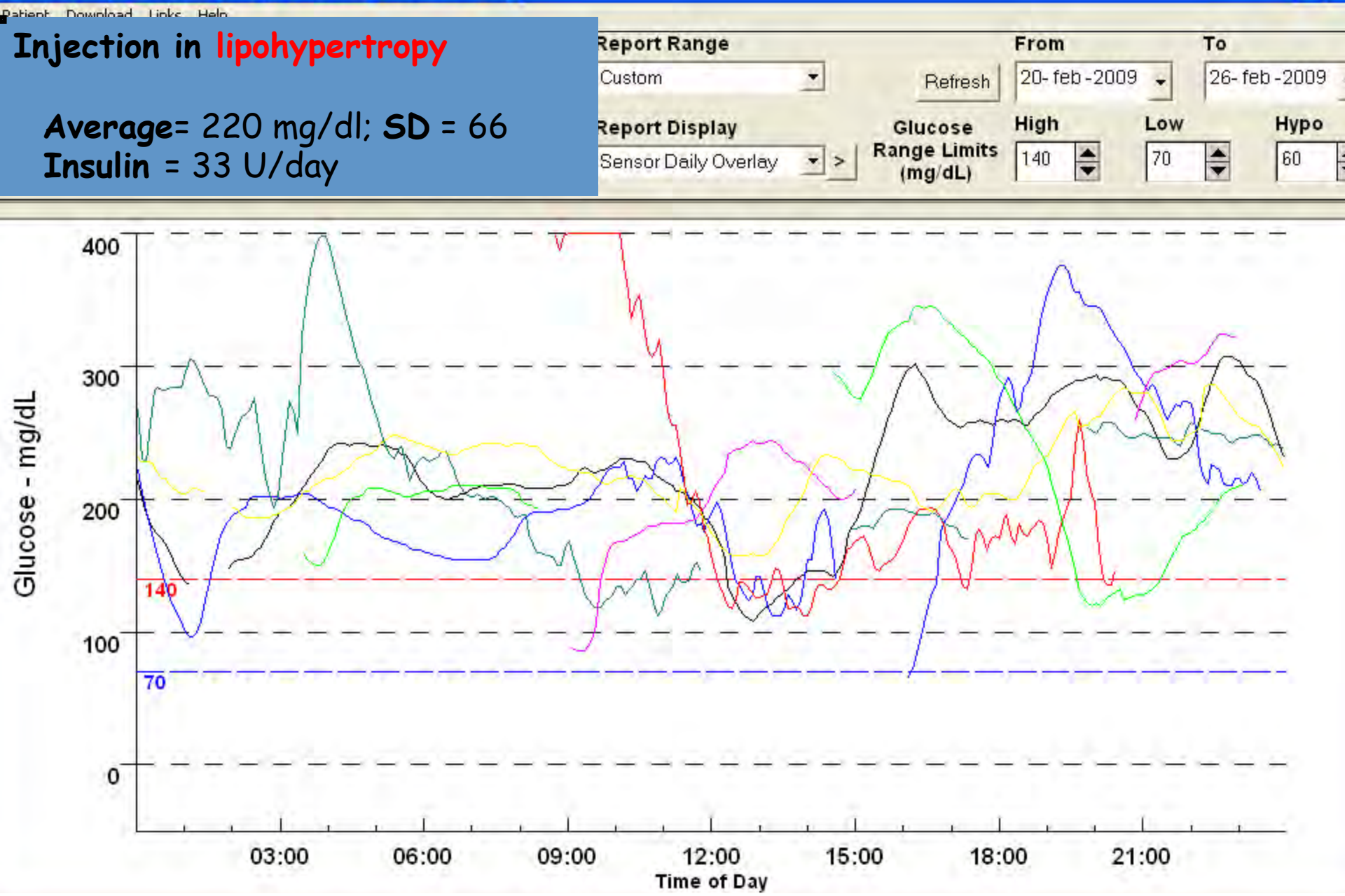
Continuous glucose monitoring system

Shows the patient not only concrete moments,

but provides a global vision of the situation

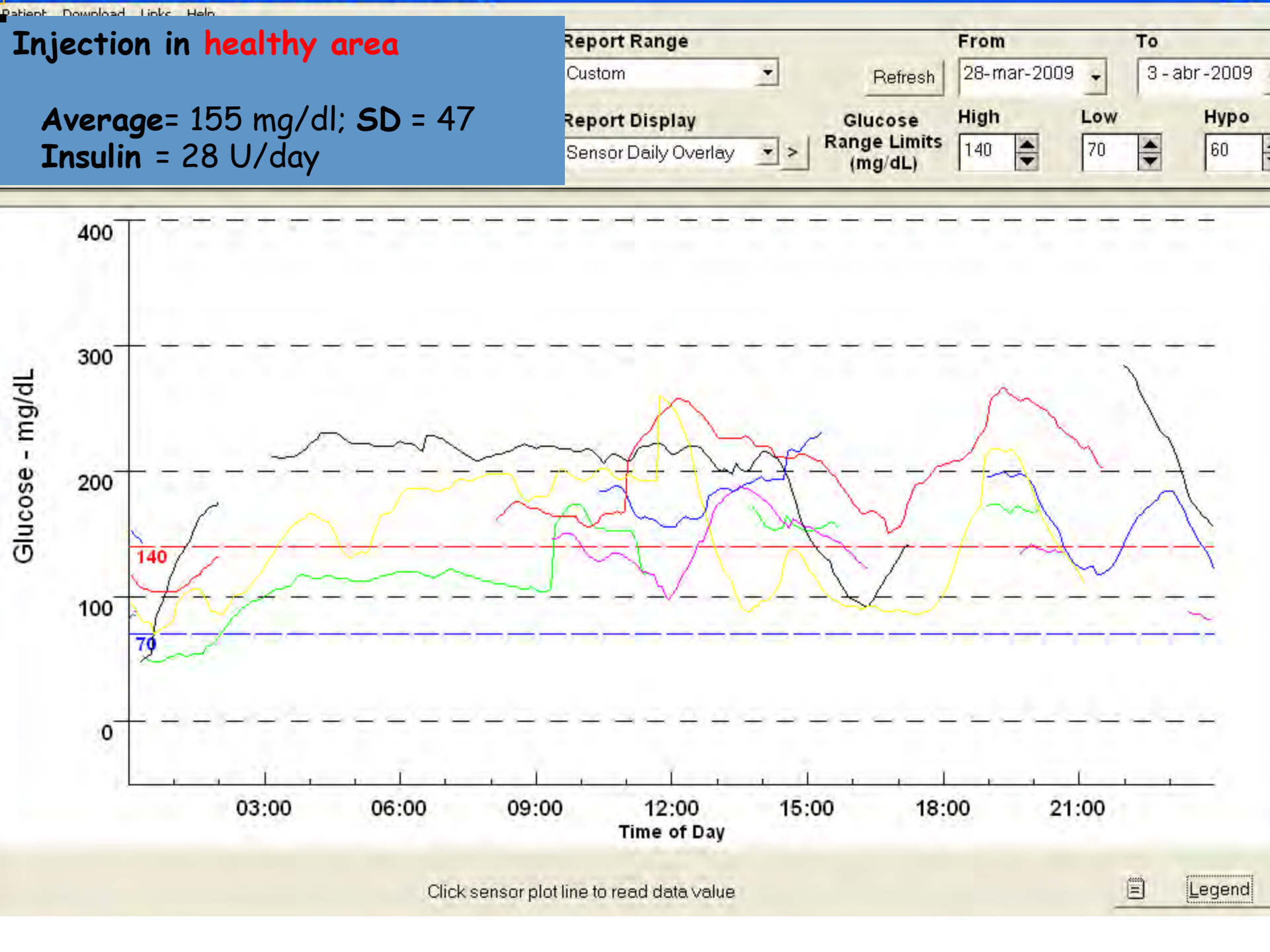
Injection in lipohypertropy

Average= 220 mg/dl; **SD** = 66
Insulin = 33 U/day



Injection in healthy area

Average= 155 mg/dl; **SD** = 47
Insulin = 28 U/day



Do you think of lipohypertrophy in patients with unstable glucose?

Seven landmark studies

1. Frequency
2. Causes
3. Histopathology
4. Absorption
5. Glucose control
6. Insulin reductions
7. Cost savings

Franzen I, J. Ludvigsson, Linköping 1997 Specific Instructions Gave Reduction of Lipomas and Improved Metabolic Control in Diabetic Children, Diabetologia Vol 40, Supplement 1: A615 (1997)

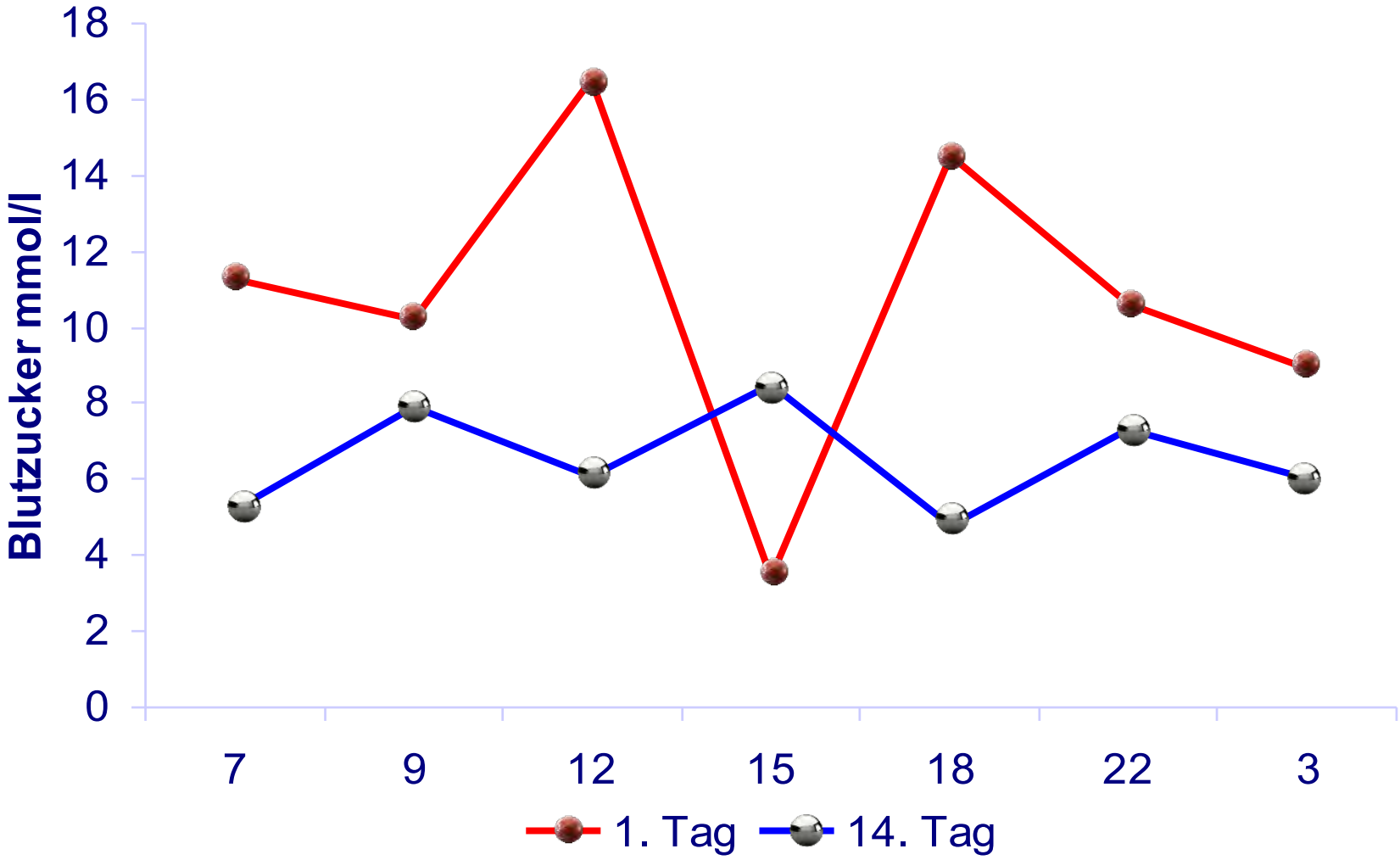
- 20 Children with clinically detectable lipos
- Received instructions:
  - Rotate!
  - Don't reuse!
- In 3 months 90% of lipos had resolved
- HbA1c was improved significantly
- Insulin requirements had decreased

Lipohypertrophy and Glucose Control in Adults

Dr. Treichel, Magdeburg
GERMANY

- 102 Adults with clinically detectable lipos
- Received instructions:
  - Rotate!
  - Don't reuse!
- 7 point glucose panel done
- Patients evaluated at Entry and 14 days later

Results


Blutzucker mmol/l
18
16
14
12
10
8
6
4
2
0
7
9
12
15
18
22
3
1. Tag
14. Tag

Seven landmark studies

1. Frequency
2. Causes
3. Histopathology
4. Absorption
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Diabetes & Metabolism

Diabetes & Metabolism 39 (2013) 445–453

Original article

Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes

M. Blanco [a], M.T. Hernández [b], K.W. Strauss [c,*], M. Amaya [d]

[a] *Novartis Pharma, Barcelona, Spain*
[b] *A.G.S. Campo de Gibraltar, Algeciras, Cádiz, Spain*
[c] *BD, POB 13, Erembodegem-Dorp 86, 9320 Erembodegem-Aalst, Belgium*
[d] *Diabetes Service Puerta de Europa, Hospital Algeciras, Cádiz, Spain*

Received 25 March 2013; received in revised form 5 May 2013; accepted 12 May 2013

Liponypertrophy and Observed Correct Rotation: Actual Results

	Lipo	No Lipo	Total
Correct	6	100	**106**
Not	262	18	**280**
Total	**268**	**118**	**386**

p= 0.0001


Cluster of injection punctures
'97 9 30

Hypoglycemia

- Of those with LH 39.1% had unexplained hypoglycemia
- For those without it was 5.9% (p=0.03)

Hypoglycemia

- Of those with LH 39.1% had unexplained hypoglycemia
- For those without it was 5.9% (p=0.03)

Glucose Variability

- Of those with LH 49.1% had glycemic variability
- For those without it was 6.5% (p=0.02)

Glucose Variability

- Of those with LH 49.1% nad glycemic variability
- For those without it was 6.5% (p=0.02)

LH and Total Insulin Dose

	Lipohypertrophy	
Dose category	Yes	No
Total Dose (mean IU/day)	56	41
Total Dose DM 1	50	42
Total Dose DM 2	62	41

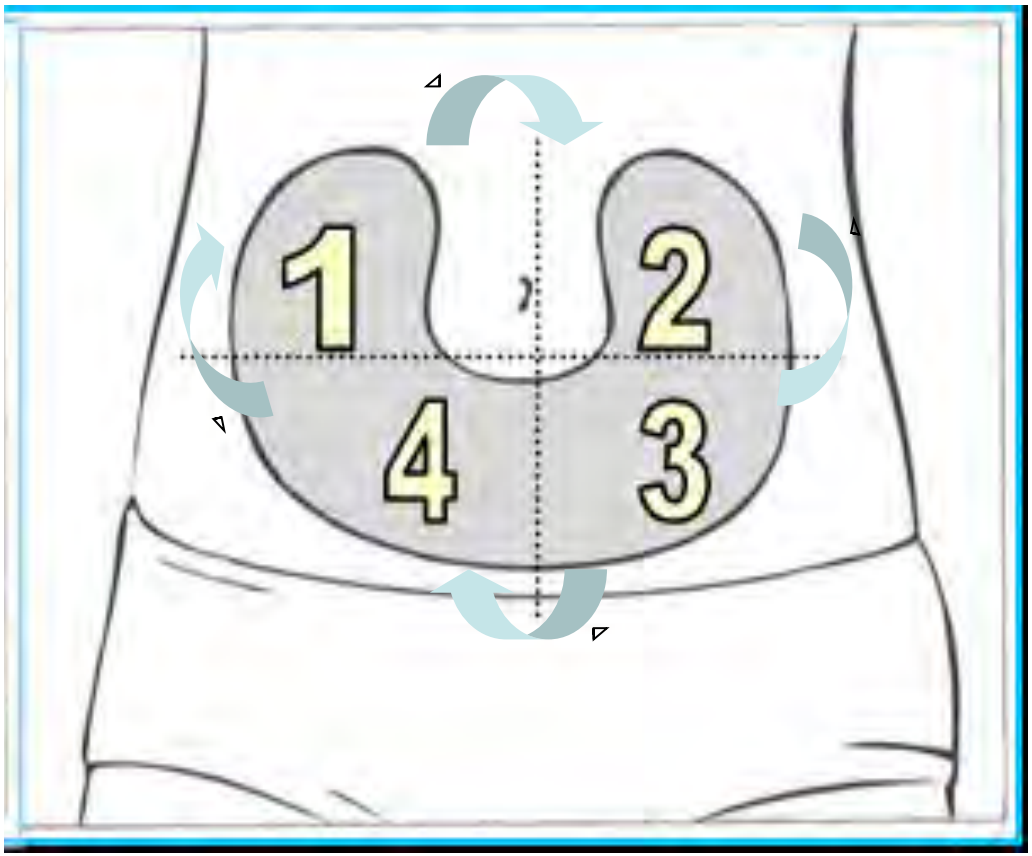
Health Economic Costs

- This 15 IU difference multiplied over the number of daily injections into LH
- Assuming a cost of 0.0243 euros/IU
- Total annual cost to the Spanish health care system of over 122 million euros.

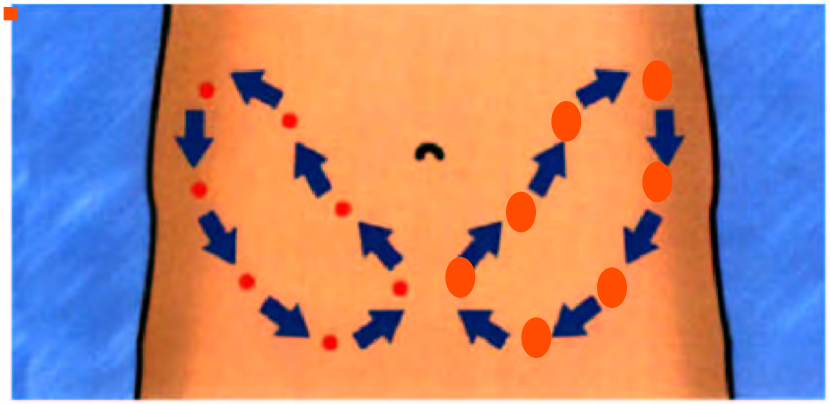
Learnings about LH

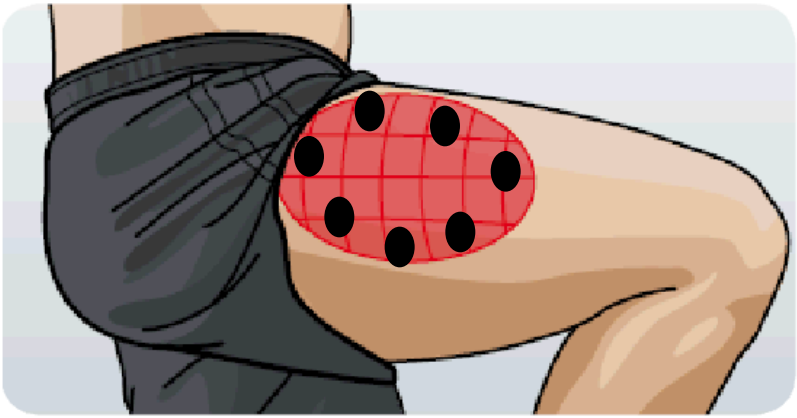
1. LH is very frequent
2. Main causes: insulin, non- rotation, reuse
3. LH distorts insulin absorption
4. LH worsens glucose control
5. LH leads to excessive and avoidable medical costs

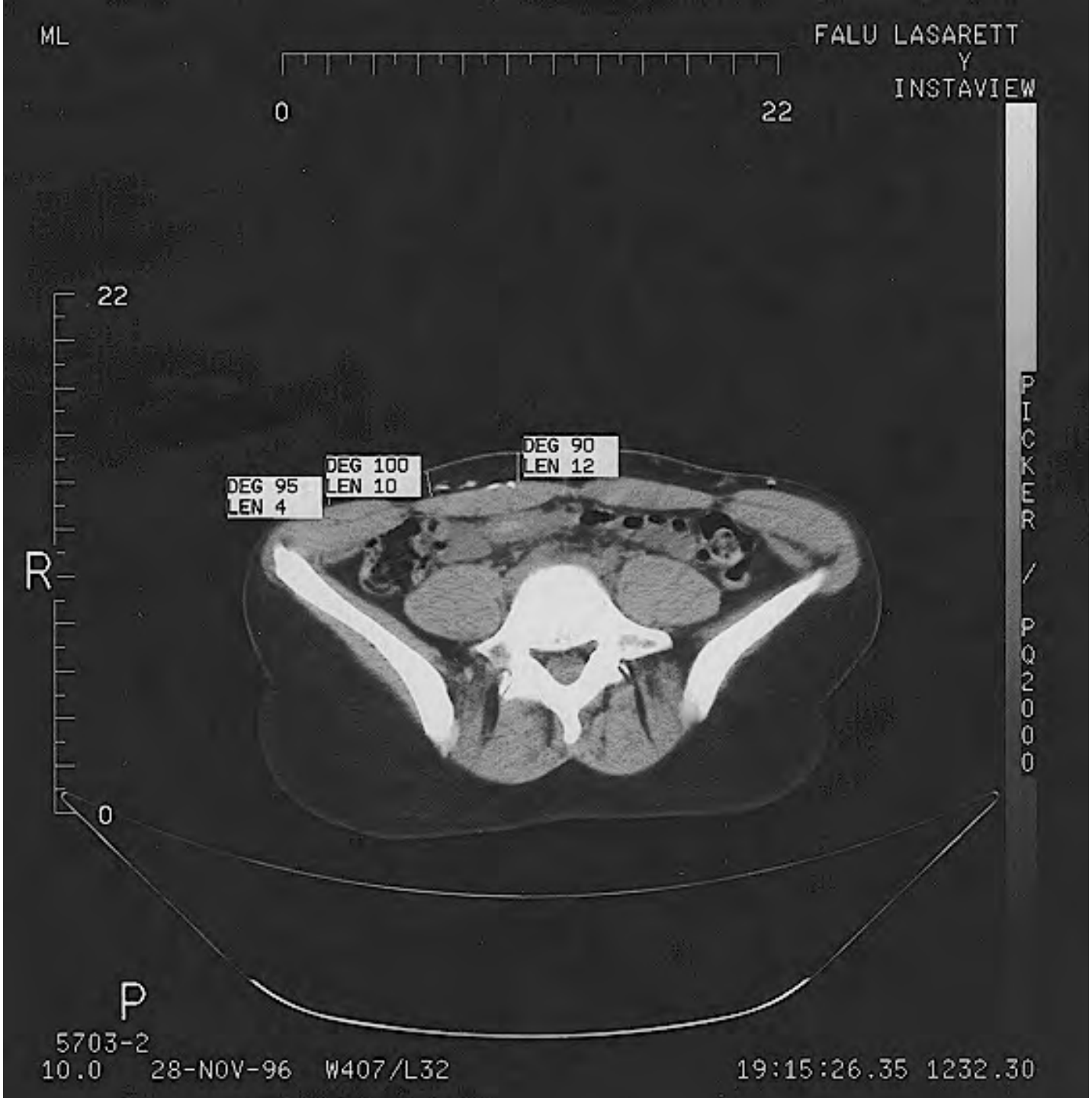
Site Rotation
AND
Rotation within Sites



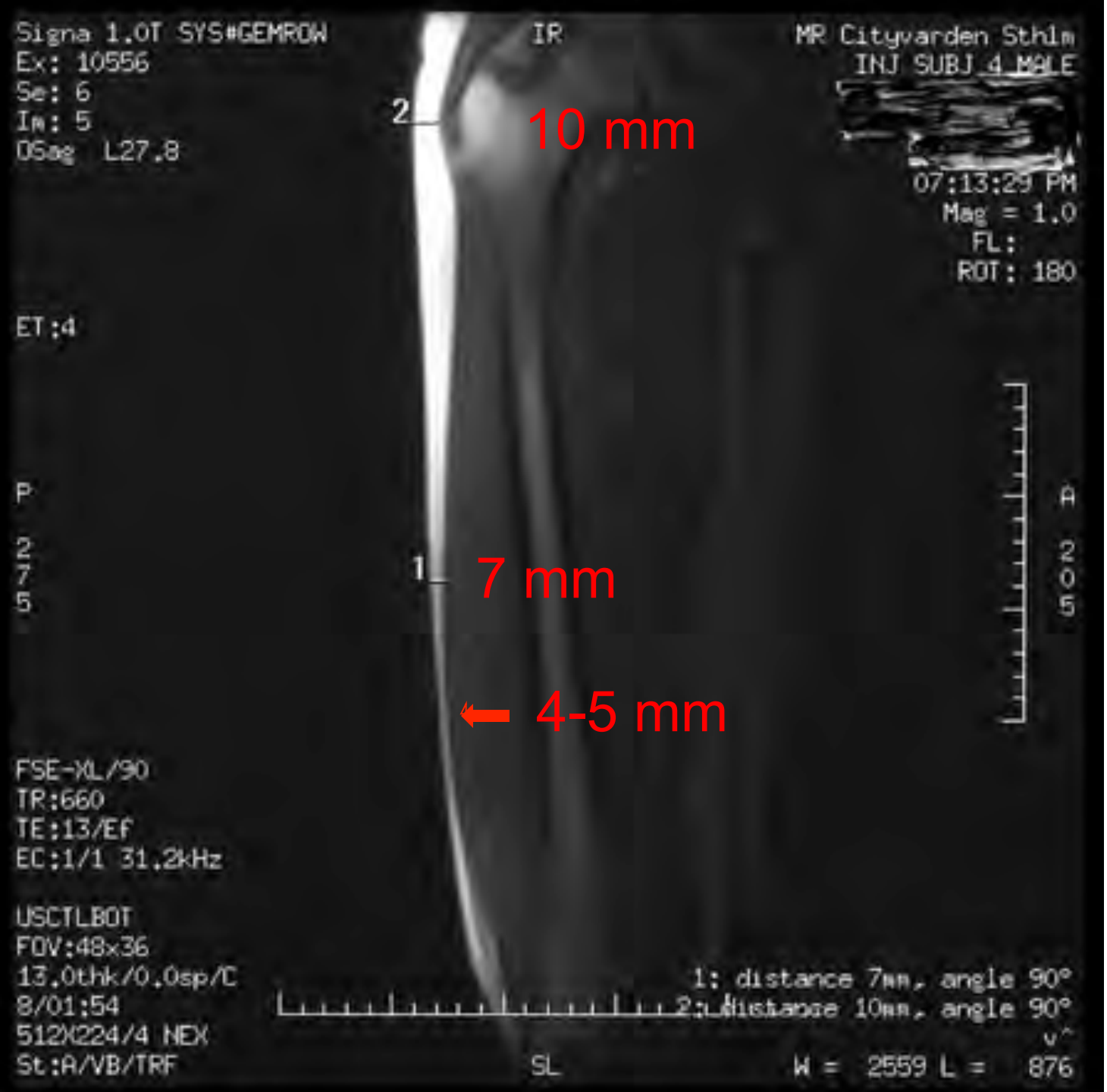
Correct Rotation = at least 1 cm between successive injections







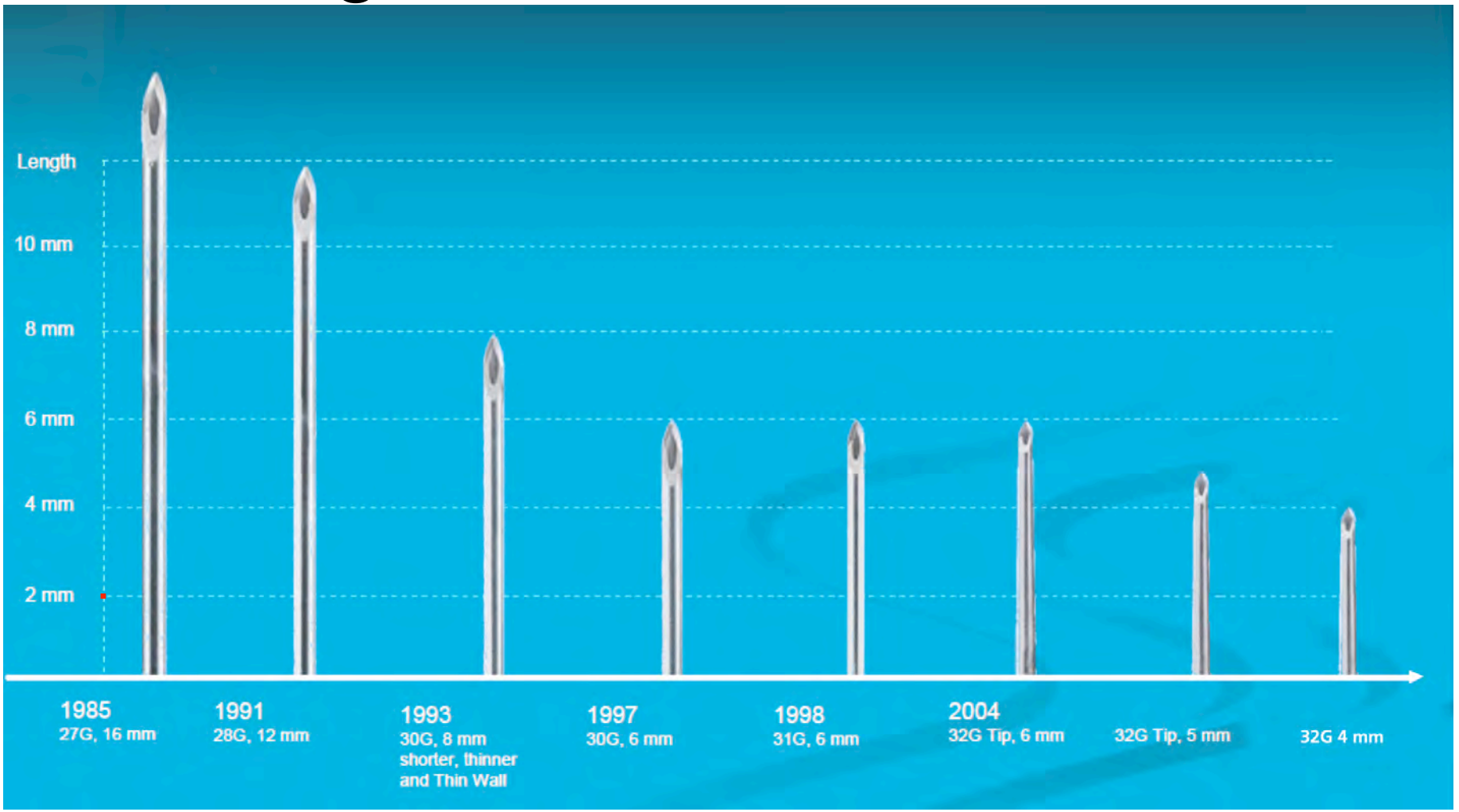
But won't this increase the risk of IM injections?



But won't this increase the risk of IM injections?

YES, unless we use shorter needles

All needles are at least twice as long as the skin is thick

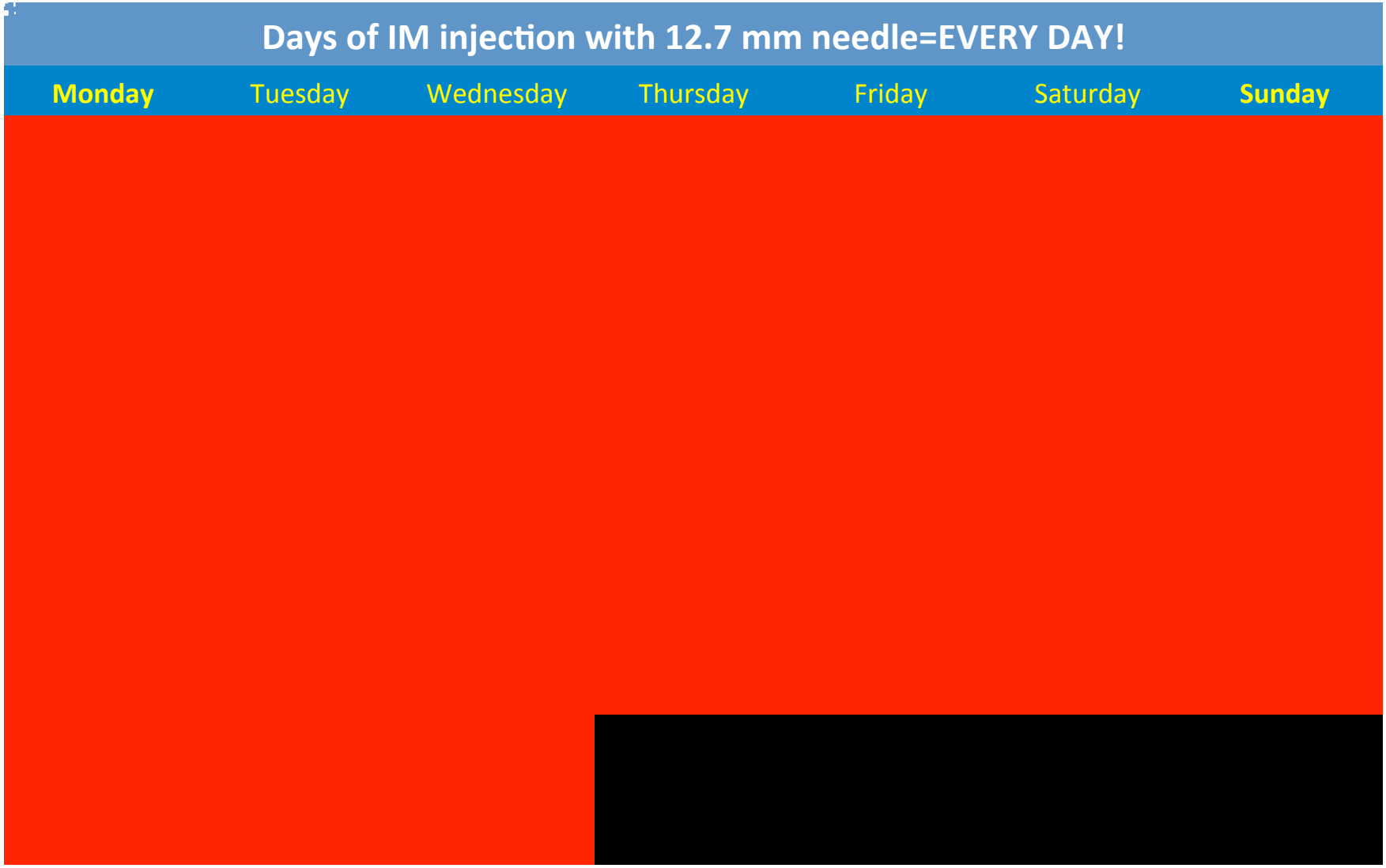


Needle length and IM injections

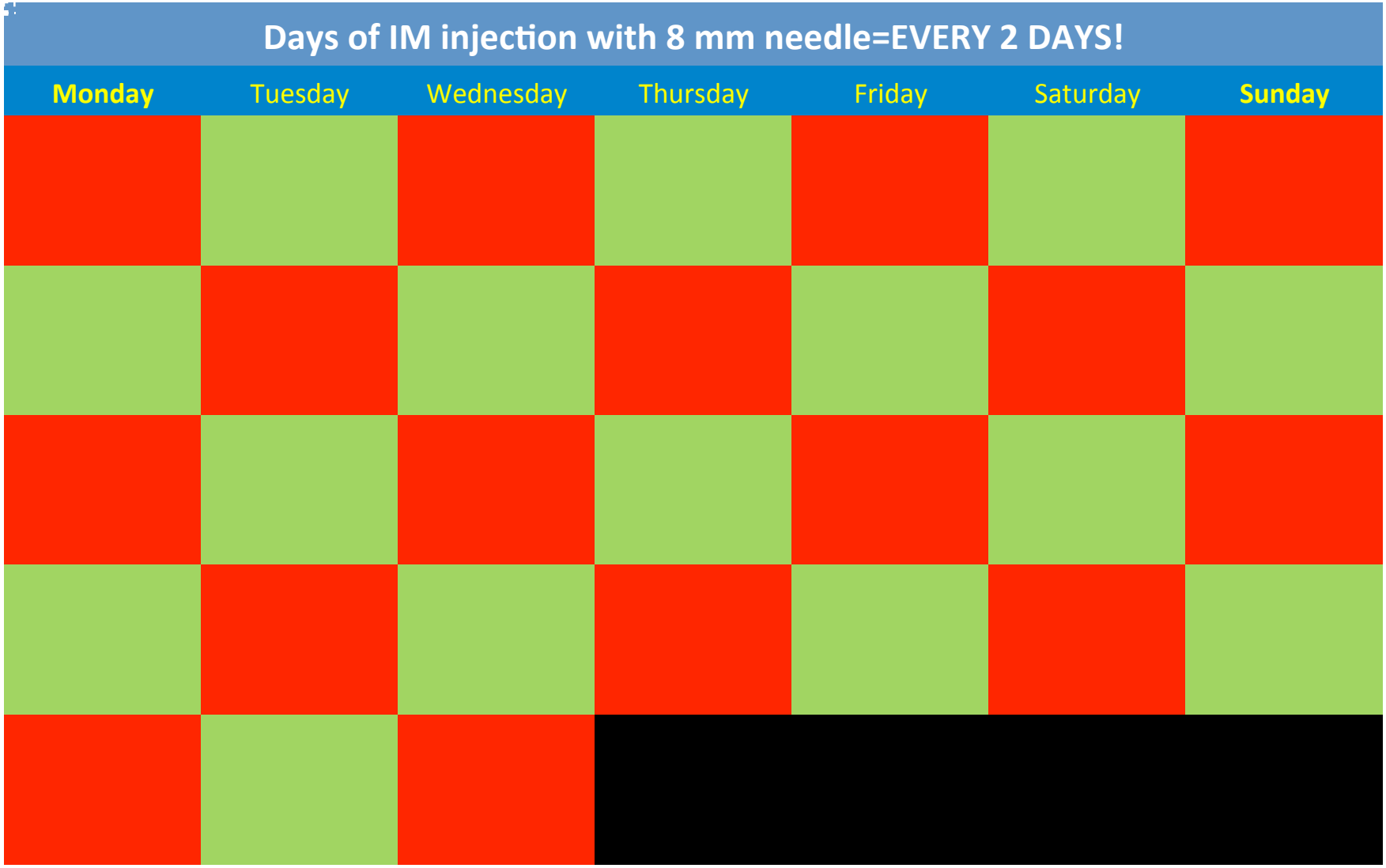
Needle Length (mm)	% IM Injections
12.7	45
8	15
6	6
5	2
4	0.4

Gibney M, et al. *Curr Med Res Opin* 2010;26:1519-30

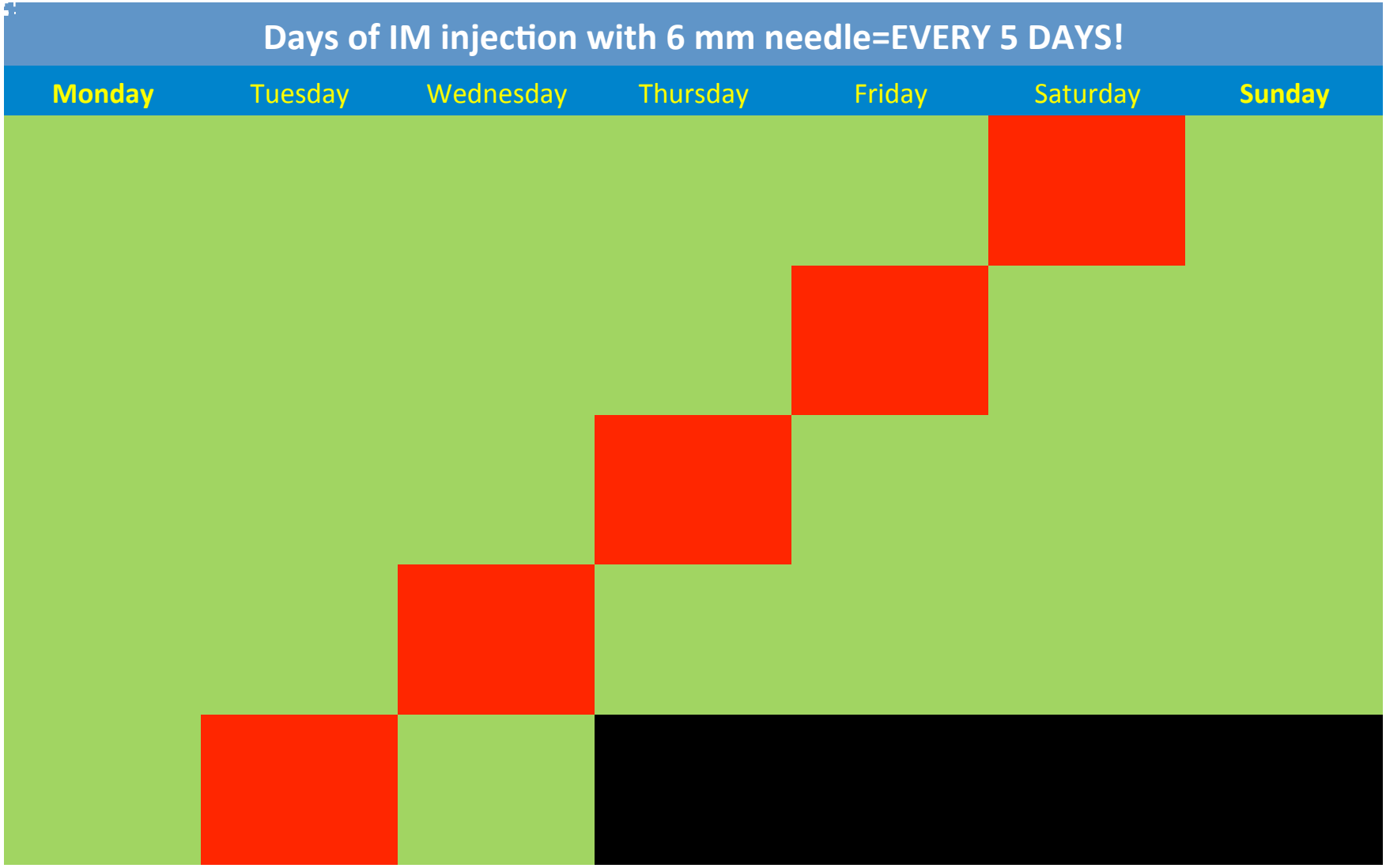
If a Patient is giving 3 injections a day, how often would he inject IM using the different needles?



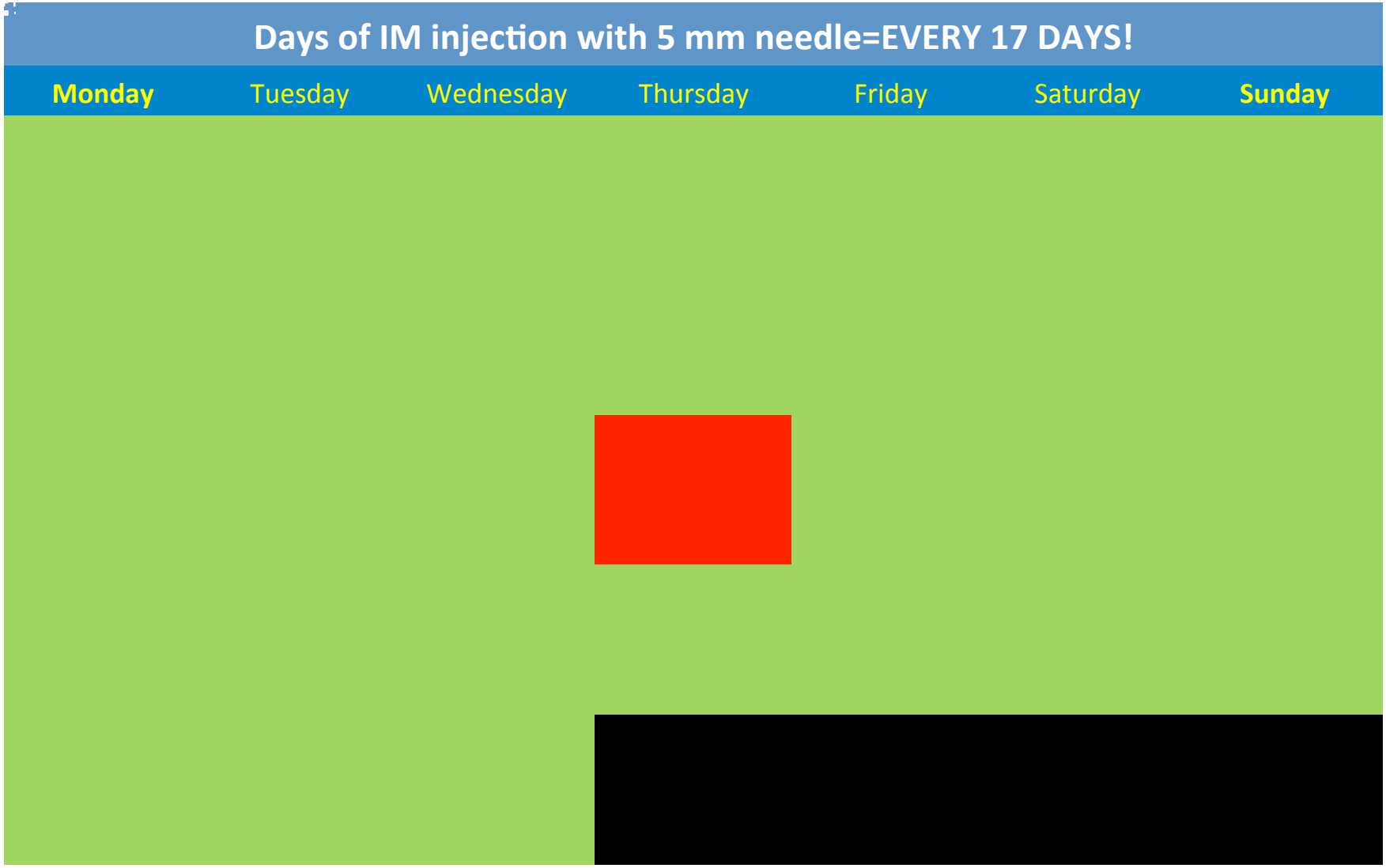
12.7 mm = EVERY DAY !



8 mm = EVERY 2 DAYS !



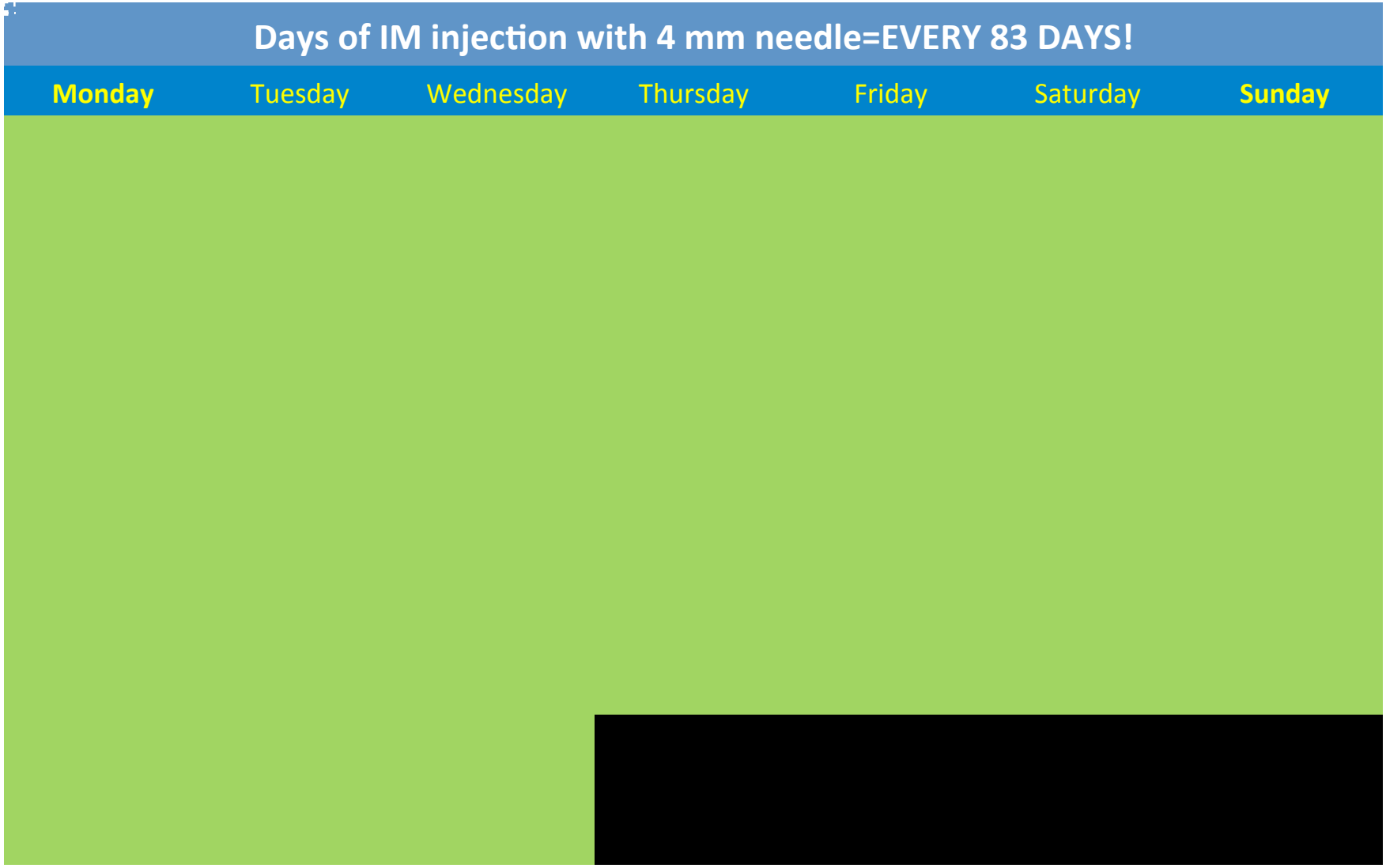
6 mm = EVERY 5 DAYS !



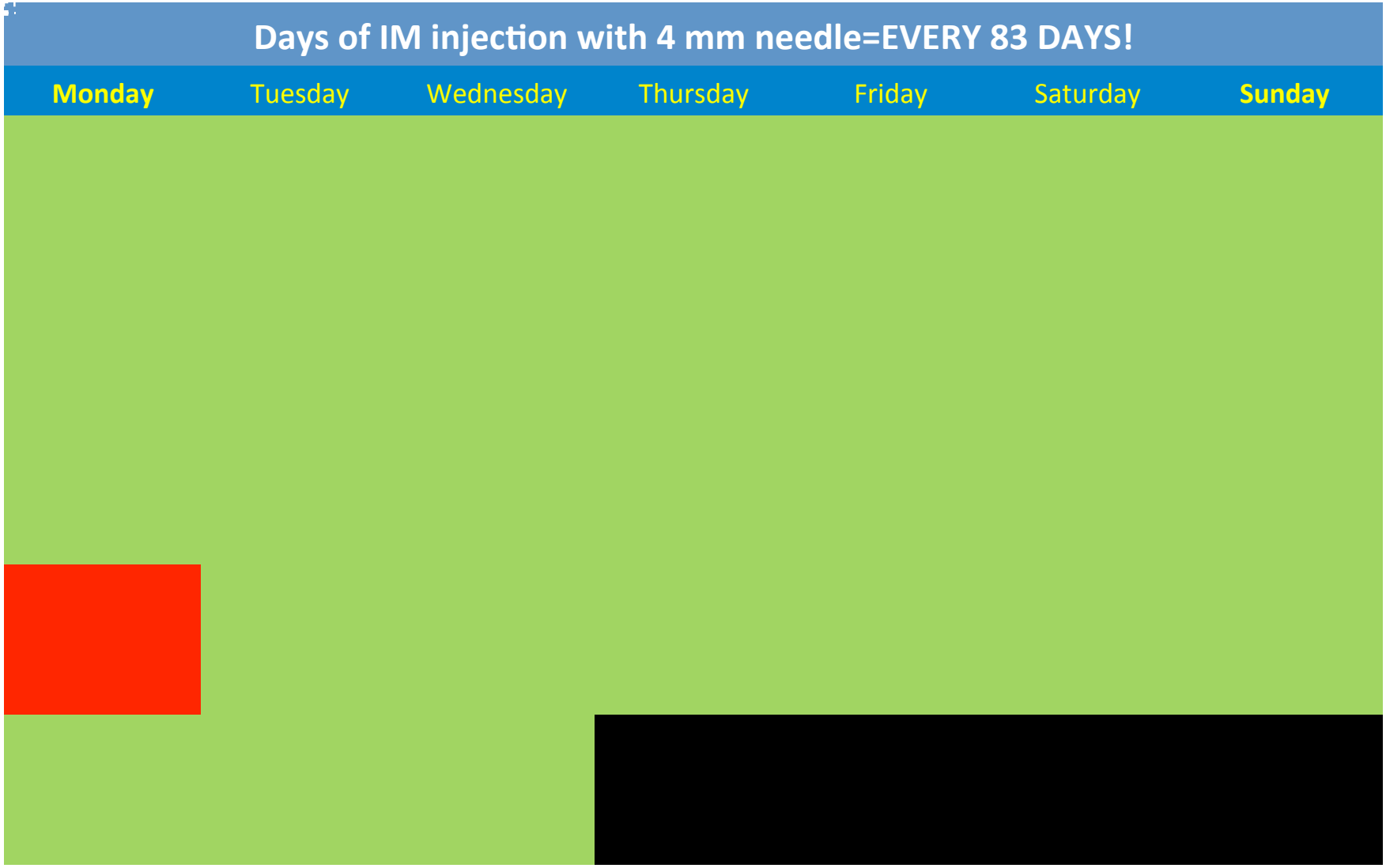
5 mm = EVERY 17 DAYS !

Days of IM injection with 4 mm needle=EVERY 83 DAYS!						
Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	**Sunday**

4 mm = MONTH 1


Days of IM injection with 4 mm needle=EVERY 83 DAYS!
Monday
Tuesday
Wednesday
Thursday
Friday
Saturday
Sunday

4 mm = MONTH 2


Days of IM injection with 4 mm needle=EVERY 83 DAYS!
Monday
Tuesday
Wednesday
Thursday
Friday
Saturday
Sunday

4 mm = MONTH 3

4 mm = EVERY 83 DAYS !

Studies Link IM injection to Hypos

1. Karges B, Boehm BO, Karges W. Early hypoglycaemia after accidental intramuscular injection of insulin glargine. *Diabet Med* 2005;**22**:1444–1445.
2. Vaag A, Handberg A, Lauritzen M, et al. Variation in absorption of NPH insulin due to intramuscular injection. *Diabetes Care* 1990;**13**:74-76.
3. Vaag A, Damgaard Pedersen K, Lauritzen M, et al. Intramuscular versus subcutaneous injection of unmodified insulin; consequences for blood glucose control in patients with type 1 diabetes mellitus. *Diabet Med* 1990;**7**:335-342.
4. Frid A, Ostman J, Linde B. Hypoglycemia risk during exercise after intramuscular injection of insulin in thigh in IDDM. *Diabetes Care* 1990;**13**:473-477.

1 hypo out of 5 is possibly linked to IM injection

How many Hypos for our Patient on 3 injections / day ?

Needle Length (mm)	Hypos due to IM injections
12.7	Every 5 days
8	Every 10 days
6	Every 25 days
5	Every 85 days
4	Every 415 days

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journal homepage: www.elsevier.com/locate/jcte

Research Paper

Optimizing insulin injection technique and its effect on blood glucose control☆

Giorgio Grassi, MD[a], Paola Scuntero, RN[b], Rosalba Trepiccioni, RN[c], Francesca Marubbi, PhD[d], Kenneth Strauss, MD[e,*]

[a] S.C.D.U. Endocrinologia, Diabetologia e Metabolismo, A.O. Citta' Della Salute E Della Scienza, Torino, Italy
[b] C.P.S.E.I. Centro Unificato Diabetologia, A.O. Citta' Della Salute E Della Scienza Torino, Italy
[c] S.C. Endocrinologia Diabetologia e Malattie del Metabolismo, Asl To2 – Ospedale Maria Vittoria, Italy
[d] BD Medical, Via delle Azalee 19, 20090 Buccinasco, MI, Italy
[e] BD, POB 13, Erembodegem-Dorp 86, B-9320 Erembodegem-Aalst, Belgium

How was this study done?

Study Design

- Patients (N=346) with diabetes from 18 ambulatory centers in Northern Italy
- Intensified and tailored Injection training
- Nature of Intervention:
  - All patients taught to rotate sites correctly to avoid lipohypertrophy
  - Switch to 4 mm needle to avoid IM
  - Instructed not to reuse needles.

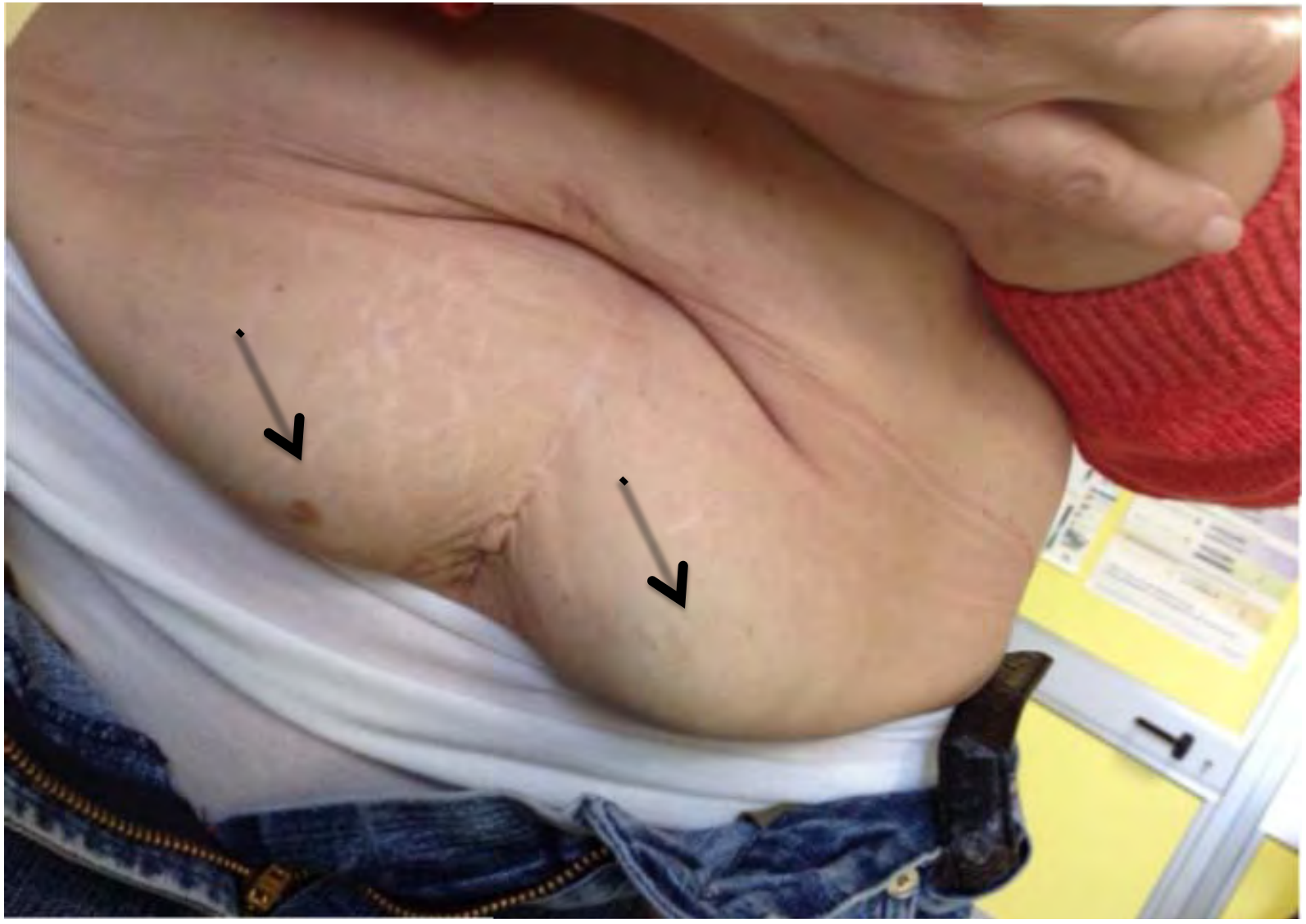
Did they see a lot of lipohypertrophy?

Lipohypertrophy is Common

	N	%
Females/Males	166/176	48.1/51.9
Visible lipohypertrophy	124	35.7
Visible lipoatrophy	18	5.2
Palpable lipohypertrophy	159	45.8
Total Lipohypertrophy*	169	48.7

Examples of visible lipohypertrophy
Bilateral upper abdomen

Examples of visible lipohypertrophy Bilateral lower abdomen



What kind of changes did they see in BG control?

Clinical Improvements

Clinical Parameter	n	Mean	Δ
HbA1c at entry	346	**8.49**	
HbA1c at 3 months	259	**7.91**	-0.58*
FBG (mg/dL)at entry	249	**186.7**	
FBG (mg/dL)at 3 months	182	**172.5**	-14.2*
TDD (IU) insulin at entry	326	**50.5**	
TDD (IU) insulin at 3 months	256	**48.5**	-2.0*
BMI** at entry	304	**28.2**	
BMI at 3 months	235	**27.7**	-0.5

*$p < 0.05$

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What kind of changes did they see in INSULIN consumption?

Clinical Improvements

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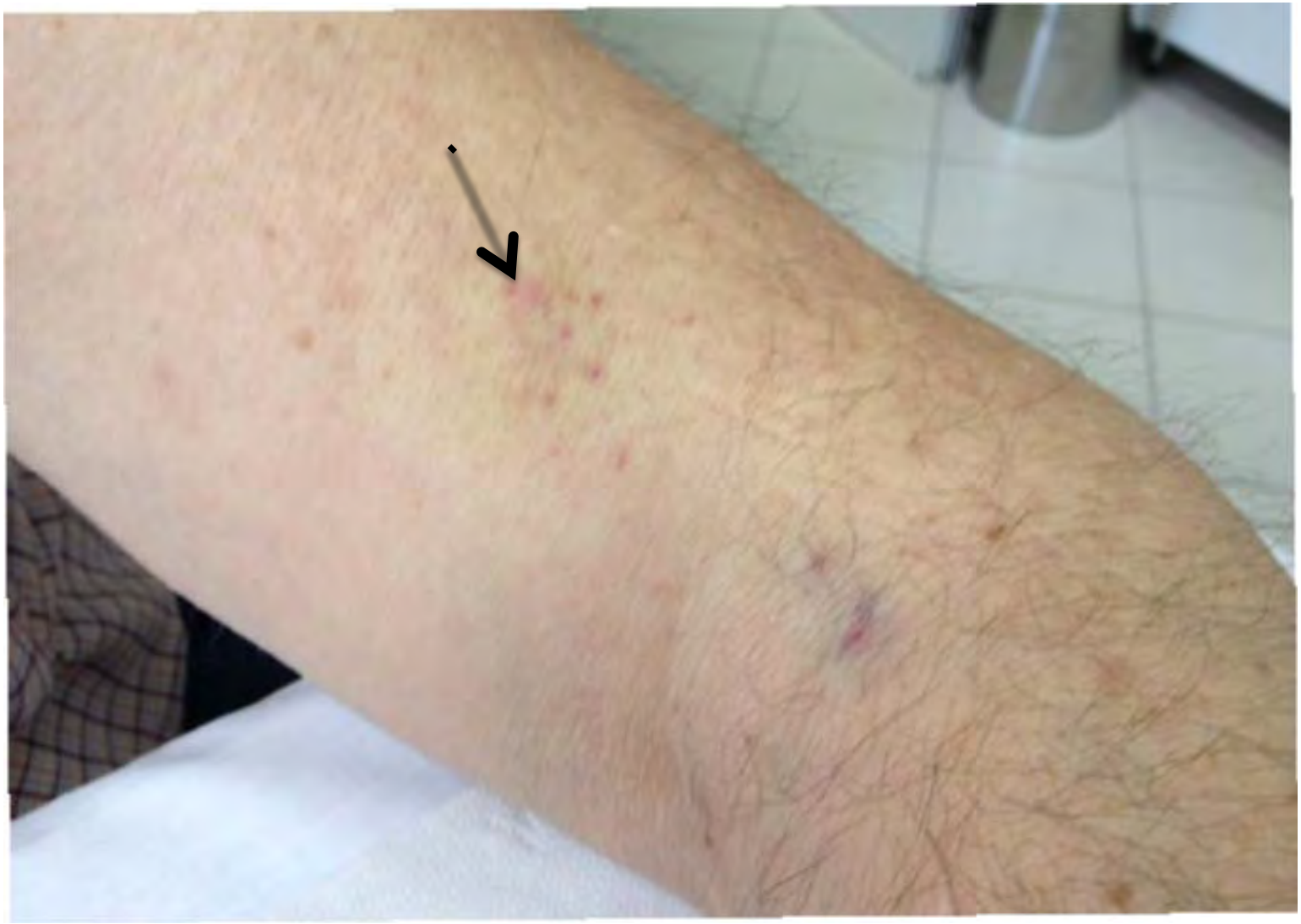
FBG (mg/dL)at entry	249	**186.7**	
FBG (mg/dL)at 3 months	182	**172.5**	-14.2*
TDD (IU) insulin at entry	326	**50.5**	
TDD (IU) insulin at 3 months	256	**48.5**	-2.0*
BMI** at entry	304	**28.2**	
BMI at 3 months	235	**27.7**	-0.5

*$p < 0.05$

What kind of behavioral changes did patients show?

Injections into inappropriate sites: elbow (see cluster of needle marks)



Injections into inappropriate sites: forearm (see bruises)

How did patient IT change?

Practice Parameter	N	%	Δ in %
Use of Pinch Up at entry	121	34.9	
Use of Pinch Up at 3 months**	31	8.9	-26.0*
<5 second dwell time after injection at entry***	133	38.3	
<5 second dwell time after injection at 3 months	21	6.1	-32.2*
5-10 second dwell time after injection at entry	193	55.6	
5-10 second dwell time after injection at 3 months	125	36.0	-19.6*
>10 second dwell time after injection at entry	50	16.7	
>10 second dwell time after injection at 3 months	162	46.7	+30.0*
Use needle only once at entry	294	84.7	
Use needle only once at 3 months	301	86.7	+2.0

How did patient perception change?

Practice Parameter	N	%	Δ in %
Consider Injection Technique VERY IMPORTANT at entry	139	40.1	
Consider Injection Technique VERY IMPORTANT at 3 months	224	64.6	+24.5*
Consider Injection Technique IMPORTANT at entry	151	43.5	
Consider Injection Technique IMPORTANT at 3 months	68	19.6	-23.9*
Consider Injection Technique SLIGHTLY IMPORTANT at entry	39	11.2	
Consider Injection Technique SLIGHTLY IMPORTANT at 3 months	9	2.6	-8.6
Consider Injection Technique NOT IMPORTANT at entry	13	3.7	
Consider Injection Technique NOT IMPORTANT at 3 months	6	1.7	-2.0

How did patient satisfaction change?

Practice Parameter	N	%	Δ in %
VERY HAPPY with current needle at entry	255	73.5	
VERY HAPPY with the 4mm needle at 3 months	314	88.9	+15.4*
OK with current needle at entry	82	23.6	
OK with the 4mm needle at 3 months	31	8.9	-14.7*
UNHAPPY with current needle at entry	5	1.4	
UNHAPPY with the 4mm needle at 3 months	3	0.9	-0.5

How long it will take to get the significant improvements through Injection Technique intervention?

Only 3 Months!

Learnings about Education

- Lipohypertrophy is present in almost half of Italian patients
- Training in Proper Injection Technique improves Control
  - HbA1c
  - Fasting Glucose
- And decreases the Total Daily Insulin Dose
- Patients don't have to wait for years to see results
- All improvements present after only 3 months

Lypohypertrophy

Picture courtesy of Nurse Ruth Gaspar, Madrid, Spain

Conclusions

1. Injection Training has a direct impact on Glucose Control and Insulin Consumption
2. Lipohypertrophy is a Huge, Largely Unrecognized Problem
3. Almost all Lipohypertrophy can be Prevented
4. Doing this would Improve Glucose Control, Reduce Insulin Consumption and Save Money
5. We Professionals must address these issues with All Injecting Patients at least once a year