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Benchmarking therapeutic drug monitoring software: ^{Corre hospitaler} A systematic evaluation of available computer tools

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Background

• Therapeutic drug monitoring (TDM) aims at predicting treatment success, failure or toxicity, and to adjust prescription in consequence¹.



What can observe ?

Objective

1. To asses and compare computer tools developed to assist clinicians in the routine individual TDM-

• Treatment is optimized by individualizing dosage regimen based on the measurement of blood concentrations.

• To maintain concentrations within a target range requires pharmacokinetic and clinical capabilities. Bayesian calculation represent a gold standard TDM approach, but requires computing assistance².

 In the last decades computer programs have been developed to assist clinicians in this assignment³.

•The development of miniaturized drug measurement methods will require embarked software to assist clinicians in dosage individualization

Pharmacokinetics

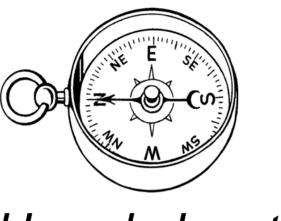


Where do I stand ?

1 2 01



Where should I go ?



TDIM For R for R For R Free Inetics Inetics Inetics Inetics Inetics Inetics

Dosage adjustment

How do I go there?

guided dosage adjustment.

2. To identify suitable specifications for the development of a novel tool designated for microplatforms.

Method

- Literature and Internet were searched to identify software
- Each program was scored against a standardized grid covering pharmacokinetic relevance, user-friendliness, computing aspects, interfacing, and storage

• A weighting factor was applied to each criterion of the grid for its relative importance

 To assess the robustness of the software, six representative clinical vignettes were processed through each of them

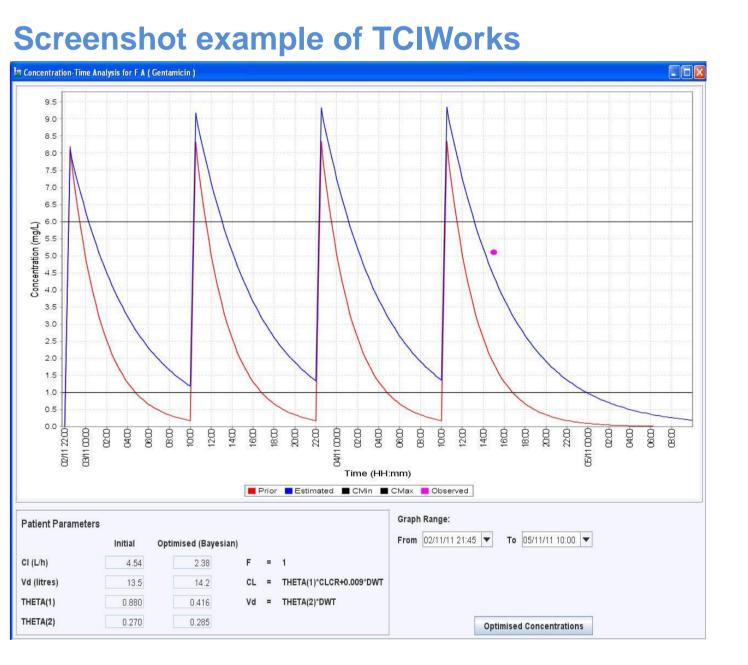
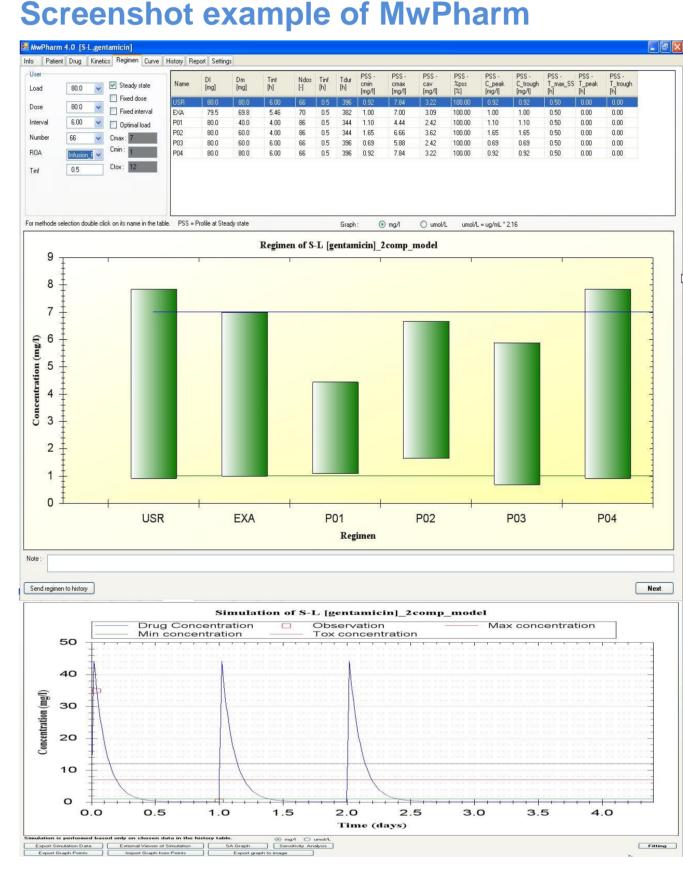


Table I : Category's and overall category's ranking (the top three programs in blue)

| | WW | ٩. | Z | 5 | | An Ki | A | Y | Kin | FU | Ki | X |
|-------------------------|----|----|---|----|----|----------|---|---|-----|----|----|----|
| General characteristics | | | | | | | | | | | | |
| User interface | 10 | 4 | 7 | 6 | 11 | 3 | 1 | 2 | 5 | 9 | 8 | 12 |
| Interfacing | 5 | 1 | 5 | 5 | 5 | 2 | 2 | 2 | 5 | 5 | 5 | 5 |
| Storage | 7 | 2 | 8 | 10 | 10 | 10 | 3 | 1 | 5 | 6 | 4 | 9 |
| Report | 10 | 1 | 7 | 8 | 12 | 9 | 2 | 2 | 6 | 5 | 4 | 10 |
| Cost | 4 | 8 | 3 | 6 | 6 | 5 | 1 | 1 | 12 | 8 | 10 | 11 |
| Computational aspects | 10 | 3 | 1 | 2 | 11 | 6 | 6 | 6 | 9 | 5 | 4 | 12 |
| Total | 10 | 3 | 4 | 9 | 11 | 8 | 1 | 2 | 6 | 7 | 5 | 12 |
| Pharmacokinetic aspects | | | | | | | | | | | | |
| Population and drug | 7 | 1 | 6 | 2 | 11 | 9 | 3 | 8 | 5 | 4 | 10 | 12 |
| Models | 1 | 3 | 2 | 9 | 10 | 8 | 7 | 6 | 4 | 5 | 11 | 12 |
| Modularity | 7 | 8 | 1 | 1 | 11 | 4 | 4 | 4 | 3 | 9 | 11 | 10 |
| Plot | 1 | 3 | 2 | 10 | 11 | 6 | 6 | 6 | 3 | 3 | 6 | 11 |
| Various | 10 | 3 | 1 | 5 | 12 | 7 | 7 | 9 | 6 | 4 | 2 | 11 |
| Total | 3 | 2 | 1 | 8 | 11 | 9 | 6 | 7 | 4 | 5 | 10 | 12 |
| Authors | | | | | | | | | | | | |
| Expertise of authors | 1 | 3 | 2 | 9 | 9 | 6 | 6 | 6 | 12 | 5 | 4 | 9 |
| GLOBAL SCORE | 6 | 1 | 2 | 9 | 11 | 8 | 3 | 4 | 7 | 5 | 10 | 12 |



Screenshot example of APK

| APK© | | | | | | | | |
|---------------------------------|---|---|---|--|--|--|--|--|
| File View Tools Help | | | | | | | | |
| Exit Report Consult Monitor | Ling Mistory Grap | l Help | | | | | | |
| Active patient list | Patien | data | Retrospective dosing | | | | | |
| Select drug Gentamicin | • e | <u>B</u> etrieve | Select analysis method | | | | | |
| | inutes after infusio before infusion | n | Steady-state peak/trough 💌 | | | | | |
| Enter serum level data | | | | | | | | |
| Dose 500 mg Infused o | iver 30 👻 minu | tes every 24 | hours for 3 doses | | | | | |
| Trough 0.27 mcg/ml dra | awn 1 minu | tes BEFORE infi | usion | | | | | |
| Peak 34.9 mcg/ml dra | awn 30 minu | tes AFTER infus | | | | | | |
| 2nd level mcg/ml dra | awn HOL | IRS after infusion | n end 🧷 Clear all | | | | | |
| Ideal dose and PK parameters | | nter recommend | led dose | | | | | |
| Ideal dose= 355 mg Q 19 hours | | 400 | mg Q 24 hours | | | | | |
| Kel=0.212 1/hr Half-life=3.3 hr | | | the second se | | | | | |
| Vd=12.3 L (0.25 L/kg) | | 30' peak = 27.9 mcg/ml +/- 2.8 Trough = 0.2 mcg/ml +/- 0.0 | | | | | | |
| CpMax= 38.8 mcg/ml CpMin= 0 | 1.3 mcg/ml | nougn= | 0.2 mcg/mi 4/-0.0 | | | | | |
| 20.10.2011 Fuchs | | Unregistered | evaluation copy | | | | | |

Results & Perspective

- 12 software tools were identified, tested and ranked, representing a comprehensive review of available software.
- MwPharm (1250 € per license) and TCIWorks (free) were best ranked tools but represent sophisticated programs.
- Numbers of drugs handled by the software vary widely (from 2 to 180).
- 8 programs offer the possibility to add new drug models based on population pharmacokinetic data.

• Bayesian computation to predict dosage adaptation based on a blood concentration (*a posteriori* adjustment) is performed by 10 tools, while 9 are also able to propose *a priori* dosage regimens, only based on individual patient covariates such as age, gender, and weight. They mostly converge to similar predictions (when possible to process).

Computer-assisted therapeutic monitoring gains growing interest and should further improve, especially in terms
of user-friendliness, institutional information system interfacing, data storage capacity and report
generation.

• This review will support the rational elaboration of a modern TDM software in the context of the ISyPeM project⁴.

Contact

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References

[1] Buclin T et al. Br J Clin Pharmacol 2012
[2] Platt DR et al. Clin Lab Med 1987
[3] Buffington DE et al. Clin pharmacokineti 1993
[4] Noverraz B et al. Poster Nano-Tera 2012