

Population-based volume kinetics of crystalloids and colloids in healthy volunteers

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Example of the control stream used in the volume kinetic model for Ringer's lactate solution.

```
$PROB RUN# 1112 (fluid kinetic model_HS_2COM)

$INPUT ID OID TIME AMT RATE DUR DV MDV SAMPLEID HB HCT PERIOD FLUID TYPE
AGE HT WT ICW ECW TBW ETRATIO HR SBP DBP MBP

$DATA 05_04_NONMEM_Bioimpedance_BP_HS.csv ACCEPT=(FLUID.EQ.1) IGNORE=#

$SUBROUTINE ADVAN13 TRANS=1 TOL=6

$MODEL COMP (VOLUME1) COMP (VOLUME2)

$PK

    TH1 = THETA(1)

    TH2 = THETA(2)

    TH3 = THETA(3)

    TH4 = THETA(4)

    TH5 = THETA(5)

    TH6 = THETA(6)

    KB = TH1 ; basal elimination rate (ml/min, 0.8 at Anesthesiology 1997;
87: 204-12)

    KR = TH2 ; renal clearance (ml/min)

    VC0 = TH3 ; baseline plasma volume (ml)

    VT0 = TH4 ; baseline interstitial volume (ml)

    KT = TH5 ; distributionl clerance (ml/min)

    KB = TH1*EXP(ETA(1))

    KR = TH2*EXP(ETA(2))

    VC0 = TH3*EXP(ETA(3))

    VT0 = (TH4+TH6** (ECW/16)) *EXP(ETA(4))

    KT = TH5*EXP(ETA(5))
```

\$DES

$$DADT(1) = RATE - KB - KR*(A(1)/VC0) - KT*(A(1)/VC0) + KT*(A(2)/VT0)$$

$$DADT(2) = KT*(A(1)/VC0) - KT*(A(2)/VT0)$$

; A1: plasma volume expansion at central compartment (VC(t) - VC0); VC(t) and VC0 mean plasma volume at any time and at baseline, respectively.

; A2: interstitial volume expansion at tissue compartment (VT(t) - VT0); VT(t) and VT0 mean interstitial volume at any time and at baseline tissue compartment, respectively.

\$ERROR

$$A1 = A(1)$$

$$A2 = A(2)$$

$$TA = A1/VC0$$

$$TB = A2/VT0$$

$$IPRED = TA$$

$$W = 1$$

$$IRES = DV - IPRED$$

$$IWRES = IRES / W$$

$$Y = IPRED + W * EPS(1)$$

\$THETA ; #5

0.8 FIX ; KB

(0, 20) ; KR

(0, 2000) ; VC0

(0, 6000) ; VT0

(0, 100) ; KT

(0, 10) ; VT0_ECW

\$OMEGA ; #3

```
0 FIX ; IIV_KB
```

```
0.3 ; IIV_KR
```

```
0.3 ; IIV_VCO
```

```
0.3 ; IIV_VT0
```

```
0 FIX ; IIV_KT
```

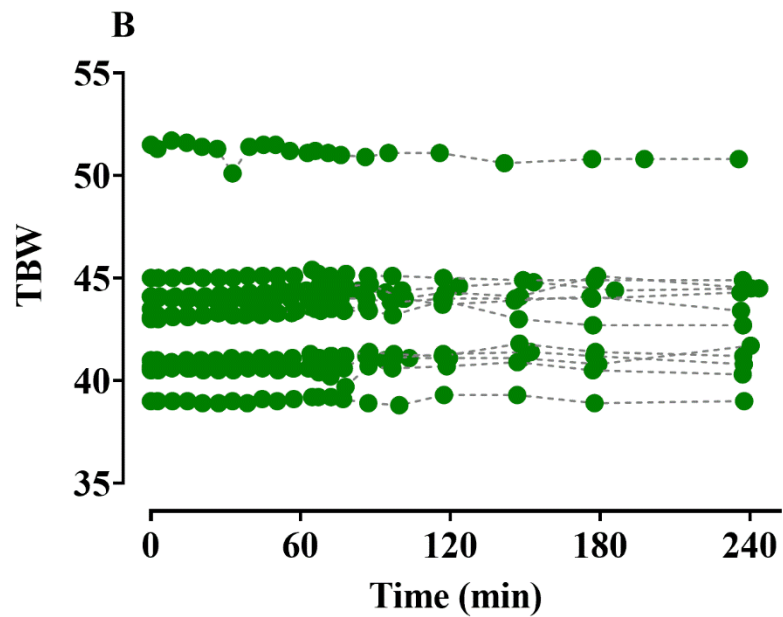
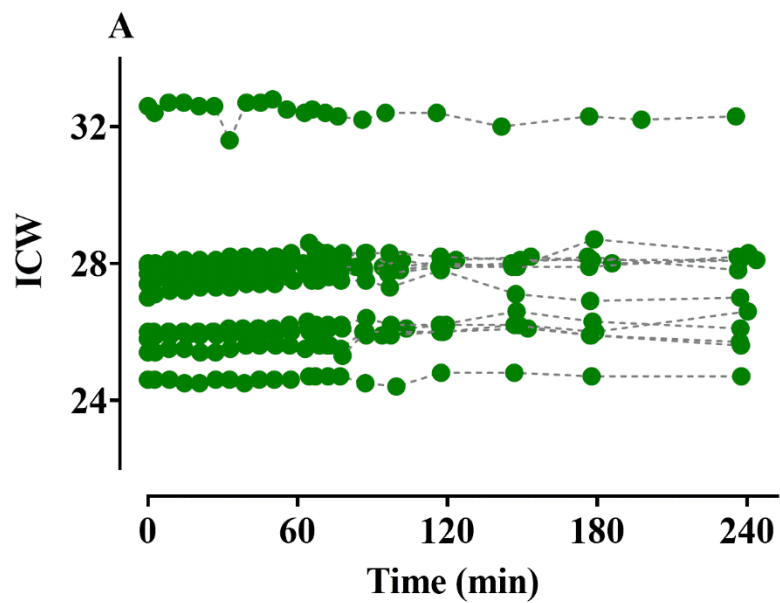
```
$SIGMA ; #1
```

```
0.01
```

```
$ESTIMATION MAXEVAL=9999 SIGL=6 NSIG=2 PRINT=5 METHOD=1 INTER NOABORT
```

```
MSFO=1112.MSF
```

```
$COVARIANCE PRINT=E
```



Supplementary figure. Changes of intracellular water (ICW; A) and total body water (TBW; B) during and after intravenous infusion of 5% dextrose water (20 mL/kg) over 1 h in 12 volunteers.