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# Impact of the automatic rounding-off function of the computerized physician order entry system on the ordering time and dose dispersion of chemotherapeutic drugs in regimens for hematologic malignancies

Kenji Tsuda[a,*], Yuko Kimura[b], Tetsuya Tanimoto[c], Yuji Takaba[d], Kensuke Okubo[e], Tomotaka Ishii[e], Yukie Takahashi[a], Tatsuo Itokawa[a], Takahiro Isshiki[a], Naoko Takei[a], Kazuhiko Kobayashi[a], Masahiko Nakagawa[d], Tsunehiko Komatsu[a]

[a] Division of Hematology, Teikyo University Chiba Medical Center, Ichihara, Japan
[b] Medical Information System Development, Teikyo University Chiba Medical Center, Ichihara, Japan
[c] Navitas Clinic, Tokyo, Japan
[d] Solutions Department 1, Medical Solutions Division, Healthcare and Educational Solutions Unit, Fujitsu Limited, Japan
[e] Metropolitan Solutions Department, Healthcare Division 2, Healthcare Solutions Unit, Fujitsu Systems East Limited, Japan

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ABSTRACT

*Introduction:* EGMAIN-GX is the computerized physician order entry system used in Japan. The automatic rounding-off of the calculated dose of chemotherapeutic drugs is an update in version 4, compared to version 2. We conducted a comparative study between EGMAIN-GX versions 2 and 4 to estimate the effect of the automatic rounding-off function on ordering time and dose dispersion.
*Methods:* Twelve hematologists ordered 5 predefined chemotherapeutic regimens most commonly used in treating hematologic malignancies, twice for each regimen.
*Results:* EGMAIN-GX version 4 significantly reduced ordering times compared to version 2 (635 s vs. 259 s, $p < 0.01$). EGMAIN-GX version 4 also yielded a significantly higher ratio of actual to ideal doses of chemotherapeutic drugs than did version 2 (1.0097 and 0.9997, respectively; $p < 0.01$) and a lower standard deviation (0.0275 and 0.0290, respectively).
*Conclusions:* The automatic rounding-off function could decrease the ordering time and dose dispersion of chemotherapeutic drugs.



## 1. Introduction

Computerized physician order entry (CPOE) is a generally accepted tool to systematically reduce the incidence of medication errors [1–3]. Chemotherapeutic drugs have a narrow therapeutic dose range, and physicians need to calculate ideal dosages meticulously according to the standardized body surface area of a patient and considering patient characteristics such as age, organ functions, infection, and disease burden. CPOE can reduce simple miscalculations [4], but prescribing chemotherapeutic regimens takes a substantial amount of time, especially in complex protocols, such as those used in treating hematologic malignancies. Furthermore, actual prescribed dosages might vary and be dispersed depending on the rounding-off methods used by each physician. Most anticancer drugs are administered according to weight (i.e., mg/kg) or body surface area (i.e., mg/m$^2$); thus, fractional parts are inevitable in most cases. Rounding off is common practice for oncology clinicians, because it makes it easy to prepare a drug by minimizing the fractional parts or drug waste that would not be used in a fixed amount vial.

EGMAIN-GX (Fujitsu Ltd., Tokyo, Japan) is one of the most popular CPOE systems in Japan. In our hospital, EGMAIN-GX version 2 had been used since 2009, and the newly introduced version 4 has been used since 2012. In version 2, the calculated dosage of each chemotherapeutic drug is shown on the typing screen (e.g., 41.6 mg), and physicians plug in a value (e.g., 41.6 mg, 41 mg, 40 mg, etc.) according to their method of rounding off. Originally, the system developers of CPOE were not involved in the doctors'

* Corresponding author. Division of Hematology, Teikyo University Chiba Medical Center, Ichihara, Japan, Postal address: 299 0111. Fax: +81 436621237.
*E-mail address:* thedod3@hotmail.com (K. Tsuda).

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**Table 1**
Details of each regimen and the rounding-off methods used in EGMAIN-GX, version 4.

| Regimen | Drug | Dose | Schedule | Round off to the nearest |
|---|---|---|---|---|
| *IDA/AraC* | Idarubicin | 12 mg/m$^2$ | Days 1–3 | 1 |
| | Cytarabine | 50 mg/m$^2$ | Days 1 & 8 | 10 |
| | | 100 mg/m$^2$ | Days 2–7 | |
| *Flu/BU*16 | Fludarabine | 30 mg/m$^2$ | Days 1–5 | 1 |
| | Busulfan | 0.8 mg/kg, 3 times | Day 2 | 1 |
| | | 0.8 mg/kg, 4 times | Days 3–5 | |
| | | 0.8 mg/kg, once | Day 6 | |
| *R − CHOP* | Rituximab | 375 mg/m$^2$ | Day 1 | 100[a] |
| | Cyclophosphamide | 750 mg/m$^2$ | Day 1 | 10 |
| | Doxorubicin | 50 mg/m$^2$ | Day 1 | 1 |
| | Vincristine | 1.4 mg/m$^2$ | Day 1 | 0.1 |
| Hyper- | Cyclophosphamide | 300 mg/m$^2$, once | Days 1 & 4 | 10 |
| | | 300 mg/m$^2$, twice | Days 2 & 3 | |
| | Doxorubicin | 50 mg/m$^2$ | Day 4 | 1 |
| | Vincristine | 2 mg | Days 4 & 11 | - |
| *R − ESHAP* | Rituximab | 375 mg/m$^2$ | Day 1 | 100[a] |
| | Etoposide | 40 mg/m$^2$ | Days 1–4 | 10 |
| | Cytarabine | 2,000 mg/m$^2$ | Day 4 | 100 |
| | Cisplatin | 12.5 mg/m$^2$ | Days 1 & 5 | 1 |
| | | 25 mg/m$^2$ | Days 2–5 | |

[a] Rituximab is rounded down to the nearest 100.

prescription right, including the rounding-off methods. Therefore, these methods were not implemented in the previous CPOE system. Notably, a new feature in version 4 is the automatic rounding-off of the calculated value to a predefined number of digits.

To estimate the effect of the automatic rounding-off function on ordering time and dose dispersion, we conducted a comparative study between EGMAIN-GX versions 2 and 4 in a mock clinical practice setting.

## 2. Methods

### 2.1. Defined mock clinical setting

Twelve hematologists ordered 5 predefined chemotherapeutic regimens for a hypothetical patient: height 165 cm, body weight 52 kg, and body surface area 1.561 m$^2$. We chose the 5 regimens that are most commonly used in treating hematologic malignancies in Japan: the IDA/AraC regimen [5], the Flu/BU16 regimen [6–7], the R-CHOP regimen [8], the Hyper-CVAD regimen [9] and the R-ESHAP regimen [10]. Details of each regimen and the exact rounding-off methods used in version 4 are shown in Table 1. The rounding-down method was used with rituximab to reduce the amount of unused partial vials, because this monoclonal antibody is expensive. To avoid an arbitrary calculation, the system developers and clinicians discussed the most appropriate way to develop the program, and the rounding-off method was defined before the trial.

For each regimen, we prescribed fixed doses of prednisolone, dexamethasone, and methylprednisolone, and those data were excluded from the analysis because they were irrelevant to the rounding-off methods. Participants entered five regimens in the same sequential order using version 2 first and then version 4: IDA/AraC, Flu/BU16, R-CHOP, Hyper-CVAD, and R-ESHAP.

### 2.2. Outcome measures

We calculated the ordering times based on the computer records and compared the median time between the 2 groups using the Wilcoxon signed-rank sum test. We also calculated the ratio of actual to ideal doses of chemotherapeutic drugs and compared the median ratios and standard deviations (SD) of the 2 groups using the Wilcoxon signed-rank sum test.

**Table 2**
Median ordering times for versions 2 and 4.

| Regimens | Ordering time | | |
|---|---|---|---|
| | Version 2 ($n$ = 12) | Version 4 ($n$ = 12) | $p$ |
| IDA/AraC, s (range) | 122 (57–213) | 22 (23–173) | <0.01 |
| Flu/Bu16, s (range) | 212 (106–271) | 53 (37–260) | <0.01 |
| R-CHOP, s (range) | 45 (22–85) | 64 (35–174) | 0.02 |
| Hyper-CVAD, s (range) | 104 (43–213) | 38 (30–226) | <0.01 |
| R-ESHAP, s (range) | 103 (35–213) | 55 (38–306) | 0.06 |
| Total, s (range) | 635 (284–826) | 259 (171–1138) | <0.01 |

**Table 3**
Median ratios of actual to ideal doses and their SDs for versions 2 and 4.

| | Version 2 | | Version 4 | |
|---|---|---|---|---|
| Drug | Median | SD | Median | SD |
| Cytarabine | 1.0000 | 0.0134 | 1.0250 | 0.0137 |
| Fludarabine | 1.0018 | 0.0388 | 1.0036 | 0 |
| Busulfan | 0.9856 | 0.0149 | 1.0096 | 0 |
| Rituximab | 1.0125 | 0.0554 | 0.9225 | 0.0810 |
| Cisplatin | 1.0250 | 0.0152 | 0.9994 | 0.0129 |
| Doxorubicin | 1.0000 | 0.0128 | 0.9994 | 0.0052 |
| Vincristine | 1.0000 | 0.0406 | 1.0000 | 0.0406 |
| Etoposide | 0.99230 | 0.0229 | 0.9609 | 0 |
| Cyclophosphamide | 1.0018 | 0.0271 | 1.0036 | 0.0028 |
| Idarubicin | 1.0000 | 0.0353 | 1.0143 | 0.0042 |
| Total | 0.9997 | 0.0290 | 1.0097 | 0.0275 |

## 3. Results

### 3.1. Ordering times

One hundred and twenty regimens with 1392 drugs were prescribed. Table 2 shows the median ordering times with versions 2 and 4. Overall, EGMAIN-GX version 4 significantly reduced ordering times compared to version 2 (635 s vs. 259 s, $p < 0.01$). Time reduction was observed consistently for all regimens except for R-CHOP and R-ESHAP.

### 3.2. Dose dispersion

Table 3 shows the median ratios of actual to ideal doses and SDs with versions 2 and 4. EGMAIN-GX version 4 yielded a significantly higher ratio than did version 2 (1.0097 and 0.9997, respectively; $p < 0.01$) and a lower SD (0.0275 and 0.0290, respectively). SDs